ABNORMAL UTERINE BLEEDING

MANAGEMENT, DIAGNOSIS, TREATMENT, AND REFERRAL

MISHA KHALIGHI MD
ADOLESCENT MEDICINE
FEBRUARY 9, 2023

ADOLESCENT MEDICINE

- Eating disorder diagnosis and treatment
- Mental health referral for medication management
- Gender-affirming care
- PrEP and STI testing and treatment
- **Reproductive and sexual health**
    - Contraception
    - **Menstrual cycle concerns**

OVERVIEW

Physiology of the menstrual cycle

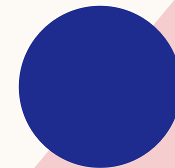
Define abnormal uterine bleeding

Heavy menstrual bleeding

Primary work-up and diagnosis

Therapies

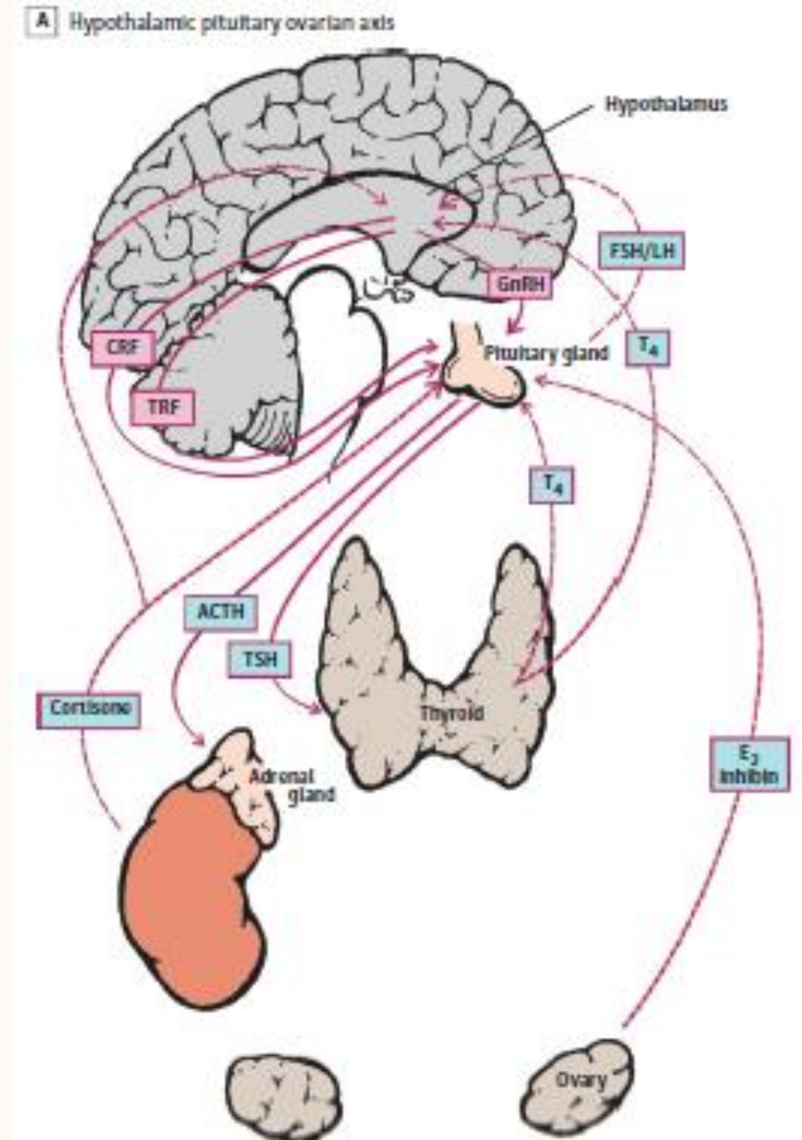
Referral



PHYSIOLOGY OF THE
MENSTRUAL CYCLE

PURPOSE:

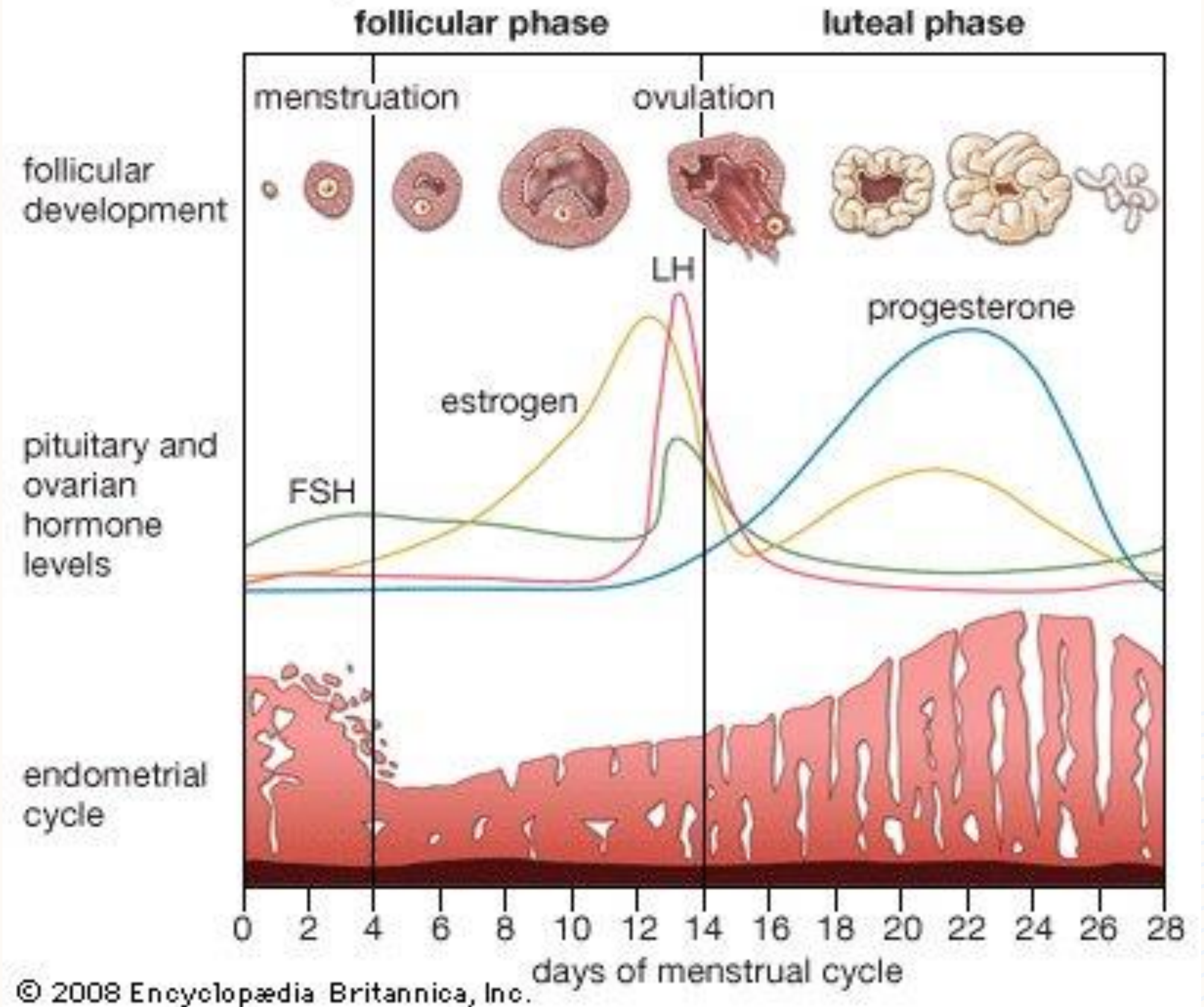
RELEASE A MATURE OOCYTE FOR FERTILIZATION AND REPRODUCTION



3. Borzutzky C, Jaffray J. Diagnosis and management of heavy menstrual bleeding and bleeding disorders in adolescents. *JAMA Pediatr.* 2020;174(2):186-194.

4 PHASES:

1. MENSTRUATION
2. FOLLICULAR PHASE
3. OVULATION
4. LUTEAL PHASE



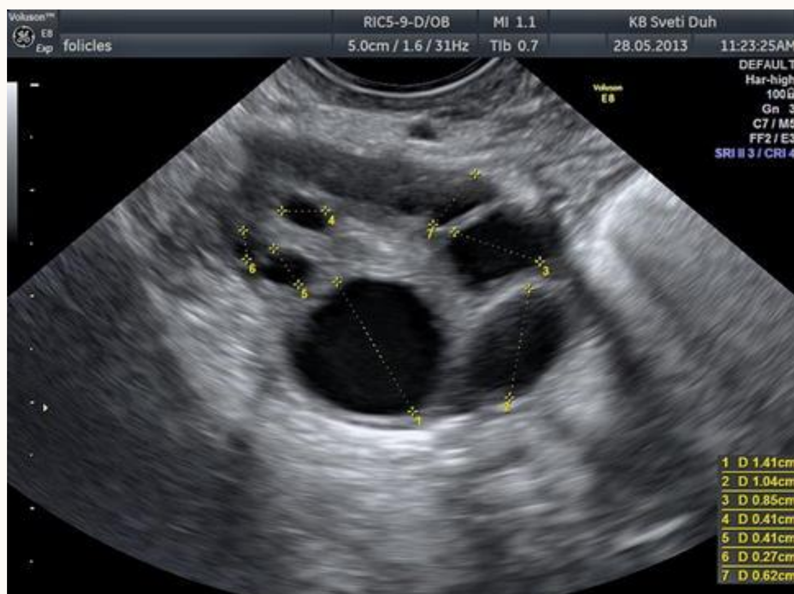
2. Welt, C. (2021) Physiology of the normal Menstrual Cycle. *UpToDate*. Retrieved August 25, 2021, from https://www.uptodate.com/contents/physiology-of-the-normal-menstrual-cycle?search=normal%20menstrual%20cycle&usage_type=default&source=search_result&selectedTitle=2~150&display_rank=2

EARLY FOLLICULAR PHASE

GnRH secretion

FSH secretion

Follicle recruitment and estrogen production



https://radiologykey.com/the-normal-ovary-changes-in-the-menstrual-cycle/

The menstrual cycle

follicular phase

luteal phase

menstruation

ovulation

follicular development

LH

progesterone

estrogen

pituitary and ovarian hormone levels

FSH

endometrial cycle

0 2 4 6 8 10 12 14 16 18 20 22 24 26 28

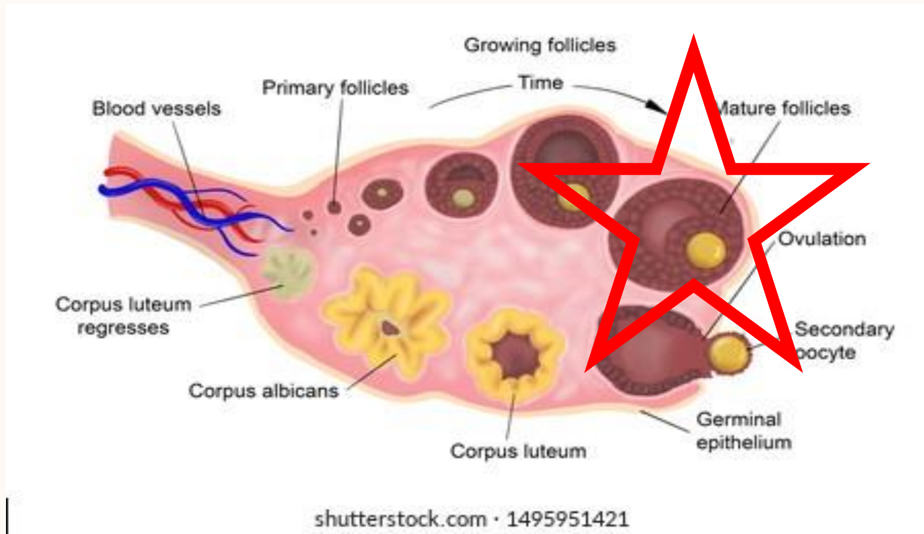
days of menstrual cycle

© 2008 Encyclopædia Britannica, Inc.

2. Welt, C. (2021) Physiology of the normal Menstrual Cycle. *UpToDate*. Retrieved August 25, 2021, from https://www.uptodate.com/contents/physiology-of-the-normal-menstrual-cycle?search=normal%20menstrual%20cycle&usage_type=default&source=search_result&selectedTitle=2~150&display_rank=2

LATE FOLLICULAR PHASE

- Estrogen rise
- Endometrial thickening
- Cervical mucous changes
- Dominant follicle



The menstrual cycle

follicular phase | luteal phase

menstruation | ovulation

follicular development

pituitary and ovarian hormone levels

FSH | estrogen | LH | progesterone

endometrial cycle

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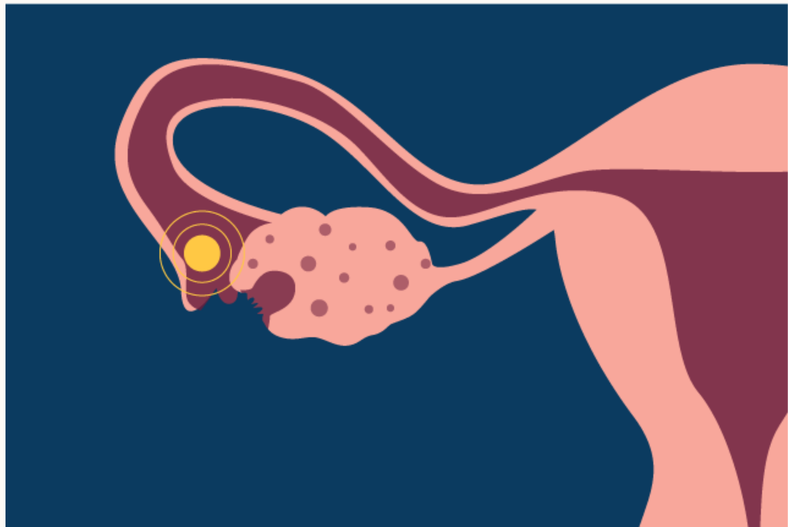
OVULATION

Estrogen peaks

Negative feedback loop switches

LH surge



The menstrual cycle

follicular phase

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menstruation

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follicular development

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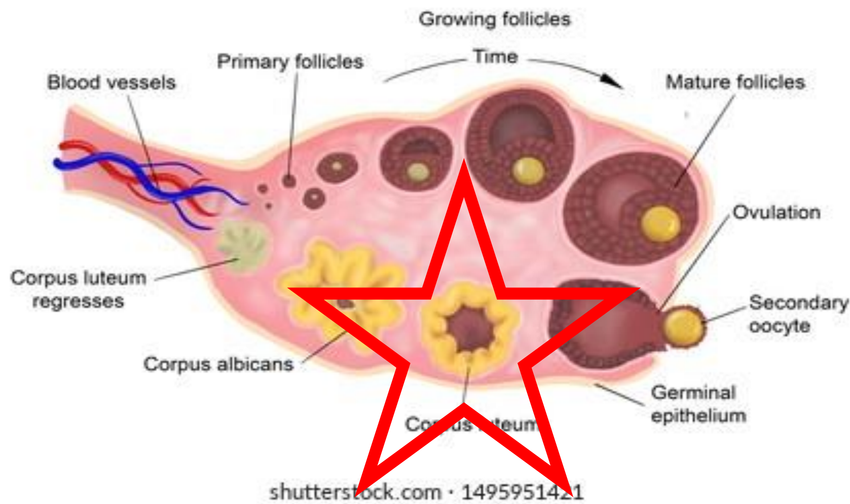
LUTEAL PHASE

Corpus luteum produces progesterone and estrogen

Without hCG, the corpus luteum degenerates



The menstrual cycle

follicular phase

luteal phase

menstruation

ovulation

follicular development

LH

progesterone

estrogen

pituitary and ovarian hormone levels

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12 – 13 YEARS-OLD

Average age in the United States at which menarche occurs[1]

15 YEARS-OLD

98% of people assigned female at birth have reached menarche[1]

50-80%

of bleeding episodes within the first 2 years of menarche are associated with anovulation[3]

1. Committee Opinion No. 651: Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign. *Obstet Gynecol.* 2015;126(6):1328
3. Borzutzky C, Jaffray J. Diagnosis and management of heavy menstrual bleeding and bleeding disorders in adolescents. *JAMA Pediatr.* 2020;174(2):186-194.

7 DAYS OR LESS

Menstrual flow duration[1]

3 – 6 PADS OR TAMPONS

Per day[1]

1. Committee Opinion No. 651: Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign. *Obstet Gynecol.* 2015;126(6):1328

ABNORMAL UTERINE
BLEEDING

ABNORMAL UTERINE BLEEDING: DEFINITION

"Menstrual flow outside of the normal volume, duration, regularity, or frequency"[5]

- Too frequent
- Not frequent enough
- Too heavy or too long

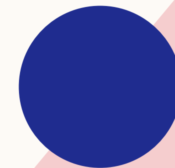
ABNORMAL UTERINE BLEEDING SUBTYPES

Amenorrhea

Oligomenorrhea

Intermenstrual bleeding

Heavy menstrual bleeding



HEAVY MENSTRUAL BLEEDING

"Excessive menstrual blood loss that interferes with a [person's] physical, social, emotional, or material quality of life."[6]

ACOG Committee Opinion, #785

6. Committee Opinion No. 785: Screening and management of bleeding disorders in adolescents with heavy menstrual bleeding. *Obstet Gynecol.* 2019;134(3):e71-e83.

ACUTE VS. CHRONIC

ACUTE

Sudden and rapid

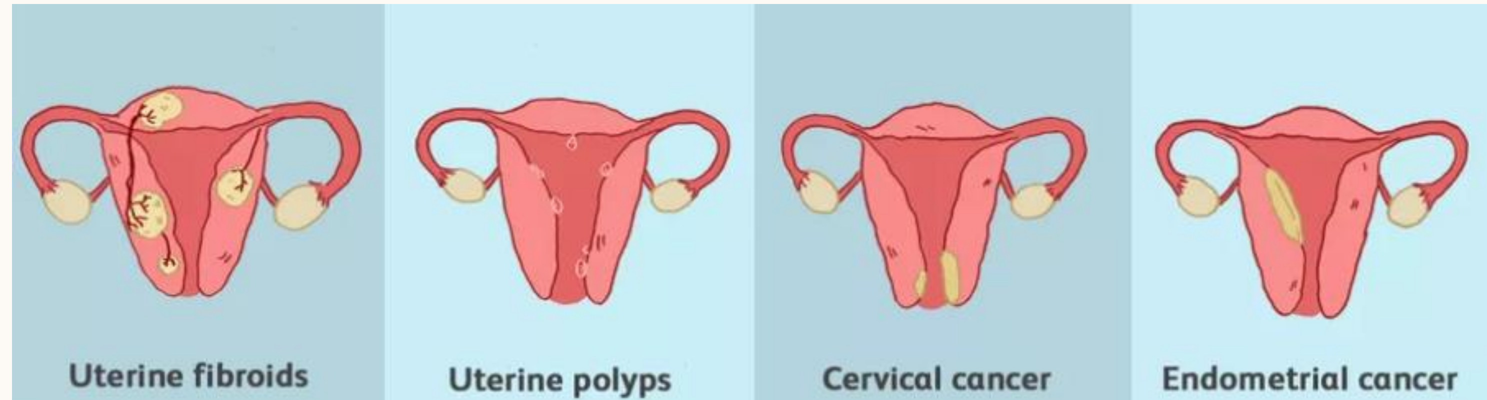
CHRONIC

Continues for >6 months

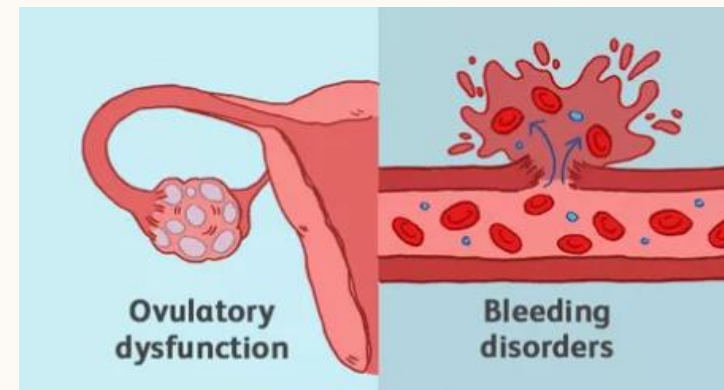
Both can lead to
Anemia
Hospitalization
Similar treatment strategies

HMB: DIFFERENTIAL DIAGNOSIS

P olyp
A denomyosis
L eiomyoma
M alignancy



C oagulopathy
O vulatory dysfunction
E ndometrial
I atrogenic
N ot otherwise specified



5. Committee Opinion No. 128: Diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol.* 2012.

HMB: THE MOST COMMON CAUSES IN ADOLESCENTS

Ovulatory dysfunction

- Anovulation
  - HPO axis immaturity
  - Thyroid dysfunction
  - Obesity
  - Stress
  - PCOS
  - Hyperprolactinemia, premature ovarian insufficiency, malnutrition → oligomenorrhea, not HMB

Coagulopathy

- 21-46% of adolescents with HMB[3]
- Inherited bleeding disorders 10-17% of women[3]
- von Willebrand disease (vWD) is the most common BD[3]

3. Borzutzky C, Jaffray J. Diagnosis and management of heavy menstrual bleeding and bleeding disorders in adolescents. *JAMA Pediatr.*2020;174(2):186-194.

HMB: WHO IS AFFECTED?

34-37%

of the general public who menstruates

74-93%

with von Willebrand's disease[3]

35-98%

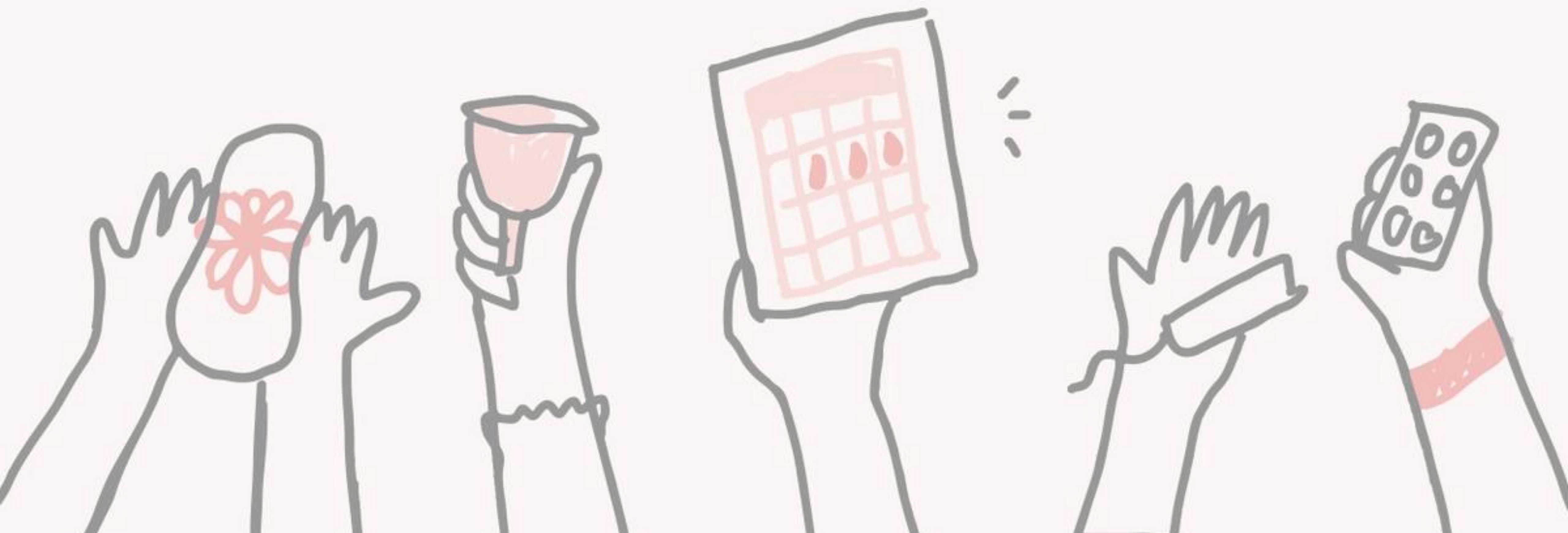
with a platelet disorder[3]

~25%

transgender and gender diverse youth experiencing breakthrough bleeding on T[7]

7. Grimstad F, Kremen J, Shim J. et al. Breakthrough bleeding in transgender and gender diverse adolescents and young adults on long-term testosterone. *J Pediatr Adolesc Gynecol*. 2021;S1083-3188(21)00191-1.

WHY IS THIS SO IMPORTANT?



$1 BILLION

Spent yearly on the treatment of HMB in the US[1]

$12 BILLION

Indirect costs through lost productivity[11]

33%

Of all gynecology visits are for HMB[12]

11. Liu Z, Doan QV, Blumenthal P, Dubois RW. A systematic review evaluating health-related quality of life, work impairment, and health-care costs and utilization in abnormal uterine bleeding. *Value Health*. 2007;10:183-94.
12. Spencer J, Louie M, Moulder J, et al. Cost-effectiveness of treatments for heavy menstrual bleeding. *Am J Obstet Gynecol*. 2017;217(5):574.e1-574.e9.

QUALITY OF LIFE

Loss of work and school days[8]

Poor physical and mental health[9]

More missed school days

More missed physical education classes

Decreased rates of sleepovers and attending others social events

Increased rates of curtailing travel plans[10]

8. Pitangui A, Gomes M, Lima A, et al. Menstruation disturbances: prevalenc, characteristics, and effects on the activities of daily living among adolescent girls from Brazil. *J Pediatr Adolesc Gynecol.* 2013;26(3):148-52.

9. Matteson K, Raker C, Clark M, Frick K. Abnormal uterine bleeding, health status, and usual source of medical care: analyses using the medical expenditures panel survey. *J Womens Health.* 2013;22(11):959-65.

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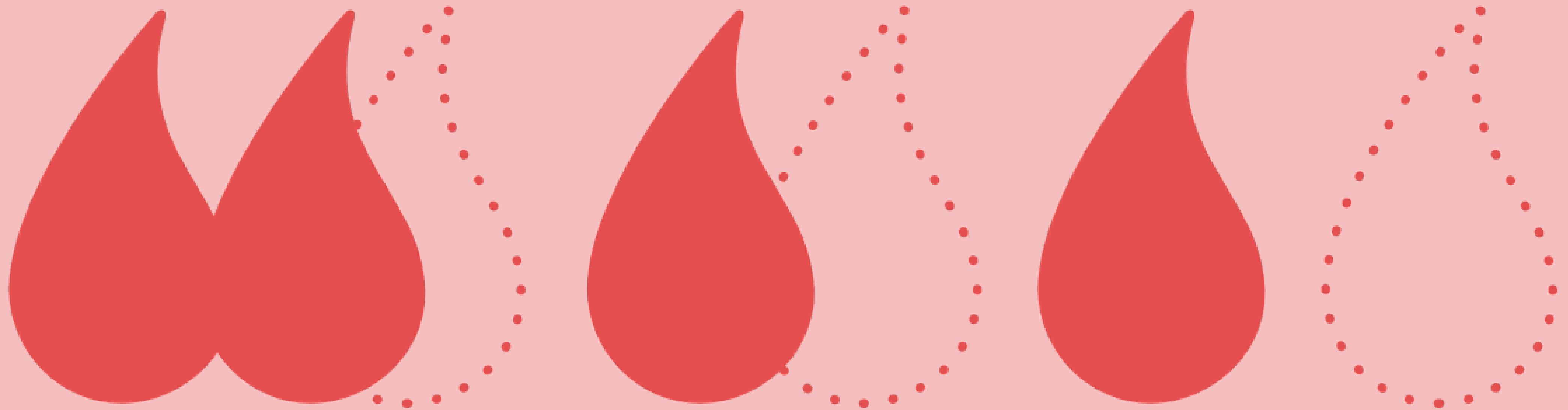


ASSESSMENT AND MANAGEMENT OF HMB

HMB: A CASE

14-year-old female presents to your office with reports of heavy menstrual bleeding for 14 days.

HMB: INFORMATION TO GATHER

Menstrual history

- Menarche
- Cycle pattern
- Length of cycle
- Duration of menstrual phase
- Pads or tampons used on heaviest days
- Clots or flooding sensation
- Pain

Personal medical history and medications

Bleeding history

- Family history of BD or blood transfusion or hysterectomy
- Personal history of bleeding/bruising/surgery

ROS

- Symptoms suggestive of thyroid dysfunction (temperature intolerance, skin/hair changes, stooling patterns, energy, appetite, weight, etc)
- Nipple discharge
- Headaches
- Visual changes
- Sexual history
- Fatigue and shortness of breath
- Pallor
- Hirsutism or acne

Contraindications to estrogen

- History of DVT, uncontrolled hypertension, migraine with aura, estrogen dependent malignancy

HMB: WORK-UP IN THE OFFICE

Assess hemodynamic status

- Vital signs and symptoms of anemia

Physical exam

- Anemia
- Petechiae and other signs of BD
- Pregnancy
- Abdominal mass

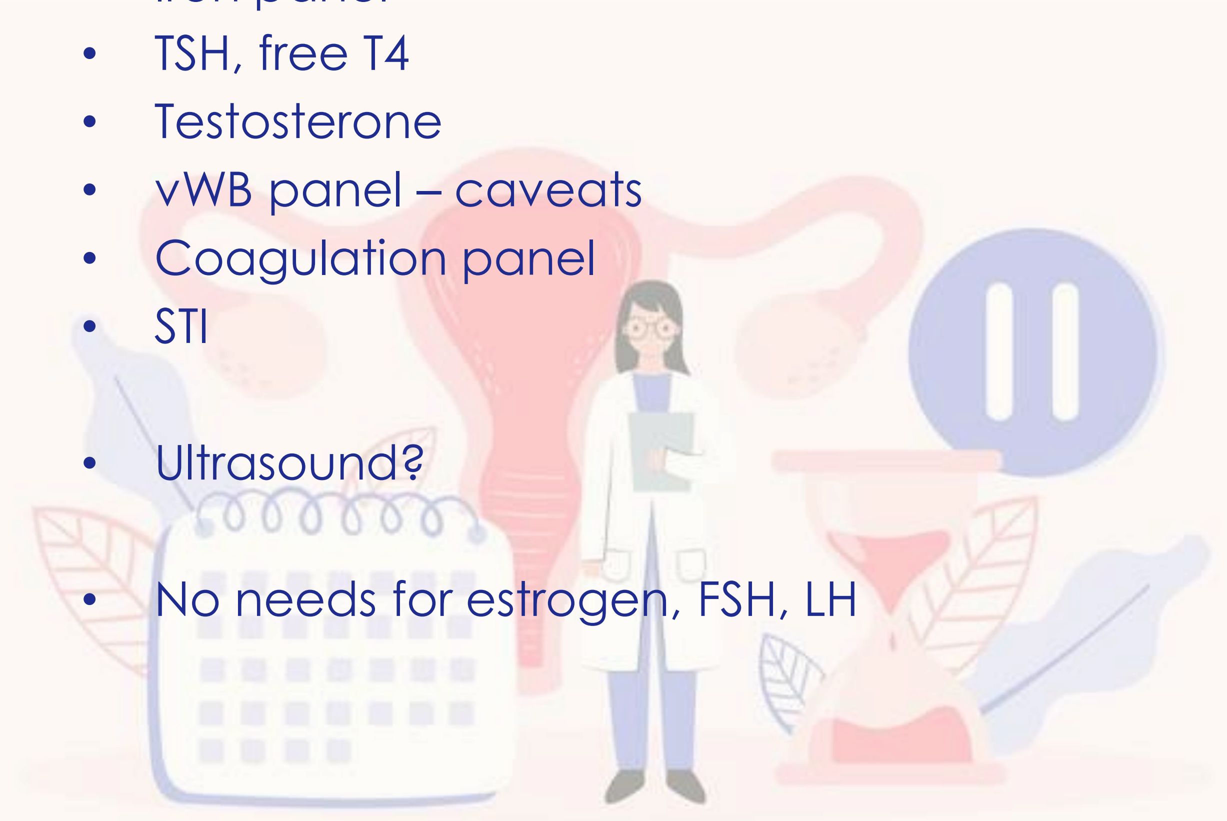
POC Hgb
POC urine HCG if sexually active

Other labs:

- CBC
- Iron panel
- TSH, free T4
- Testosterone
- vWB panel – caveats
- Coagulation panel
- STI

- Ultrasound?

- No needs for estrogen, FSH, LH



MANAGEMENT OF ACUTE HMB

HORMONAL		NON-HORMONAL	
PROGESTINS	**ESTROGEN**	**NSAIDS**	**HEMOSTATIC MEDICATIONS**
Induces endometrial atrophy Reduces proliferation of the endometrium	Induces vasospasm in the endometrium More predictable bleeding patterns when used as a cyclic OCP	Decreases prostaglandin synthesis	Tranexamic acid (antifibrinolytic) Aminocaproic acid (antifibrinolytic) DDAVP (synthetic vasopressin)

HORMONAL MEDICATIONS

PROGESTINS

Medroxyprogesterone acetate (PO or IM)

Norethindrone (PO)

Drospirenone (PO)

Levonorgestrel IUD

Nexplanon?

ESTROGEN

Intravenous conjugated equine estrogen (IV-CEE)

COMBINED

Combined oral contraceptives (COCs)

Vaginal ring

Topical patch

DOSING AND INITIATION OF TREATMENT FOR ACUTE HMB

High dose progestin taper

- **Medroxyprogesterone acetate 20mg PO TID x 7 days followed by 20mg PO daily x 21 days, then 10mg PO daily for maintenance**
- Norethindrone 10-30mg PO daily 7 days followed by norethindrone 10mg PO daily for maintenance (with further potential decrease to 5 or 2.5mg PO daily)
- High doses drospirenone 4mg – 2-4 tabs daily x3-4 days with taper

High dose combined contraceptive taper

- Monophasic
- Taper: 2 pills BID for 3-4 days, 3 pills daily for 3 days, 1 pill BID for 2 weeks, 1 pill daily
  - Could you start with 1 pill BID? Sure.

Intravenous conjugated equine estrogen

- 25mg IV q4 hours x24 hours
- Must add a maintenance medication

Adjunctive NSAIDs

- Ibuprofen 800mg at onset, followed by 600mg q8 hours x3-5 days
- Naproxen 500mg at onset and 3-5 hours later, followed by 500mg BID x5 days

14. Hatcher RA, Nelson AL, Trussell J, et al. *Contraceptive Technology*. Atlanta, GA: Managing Contraception, LLC; 2018.

DOSING AND INITIATION OF TREATMENT FOR ACUTE HMB

Antifibrinolytics

- Studies show tranexamic acid to be better tolerated than aminocaproic acid
- It is FDA approved for the treatment of HMB
- Tranexamic acid 10mg/kg IV or 500mg IV q8h (faster onset than PO)
- Tranexamic acid 1300mg PO TID x5 days

- No maintenance between cycles
- Expensive

15. James, AH. Diagnosis and management of women with bleeding disorders - international guidelines and consensus from an international expert panel. *Haemophilia*. 2011;17:3-5. doi:10.1111/j.1365-2516.2011.02557.x

DOSING AND INITIATION OF TREATMENT FOR CHRONIC HMB

Progestins

- Medroxyprogesterone acetate 10mg PO daily
- Norethindrone 2.5-10mg PO daily
- Depo-medroxyprogesterone acetate 150mg IM x1 monthly x3 months followed by injection every 11-13 weeks for maintenance
- Drospirenone 4mg PO daily (aka Slynd)
- 52mg levonorgestrel-releasing IUD

Combined contraceptives

- One FDA approved pill: Natazia (estradiol valerate-dienogest)
- Any other COCs (even low dose EE pills show reduction in blood loss)
- Vaginal ring or patch

14. Hatcher RA, Nelson AL, Trussell J, et al. *Contraceptive Technology*. Atlanta, GA: Managing Contraception, LLC; 2018.

DOSING AND INITIATION OF TREATMENT FOR CHRONIC HMB

Antifibrinolytics

- Tranexamic acid 1300mg PO TID x5 days

NSAIDs

- Ibuprofen 800mg at onset followed by 600mg q8h x3-5 days
- Naproxen 500mg at onset, again 3-5 hours later, then 500mg BID x5 days

Multicenter Study > J Adolesc Health. 2022 Aug;71(2):204-209.
doi: 10.1016/j.jadohealth.2022.02.018. Epub 2022 Apr 13.

Does a Bleeding Disorder Lessen the Efficacy of the 52-mg Levonorgestrel-Releasing Intrauterine System for Heavy Menstrual Bleeding in Adolescents? A Retrospective Multicenter Study

Misha Khalighi [1], Allison P Wheeler [2], Oluyemisi A Adeyemi-Fowode [3], Peter A Kouides [4], Ramon A Durazo-Arvizu [5], Kristina Haley [6], Candice M Dersch [7], Angela C Weyand [8], Maureen K Baldwin [9], Claudia Borzutzky [10]

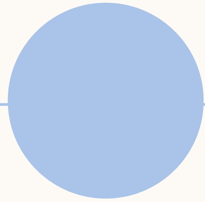
Affiliations + expand

PMID: 35430143 PMCID: PMC9329177 (available on 2023-08-01)
DOI: 10.1016/j.jadohealth.2022.02.018

Project done, manuscript in process:

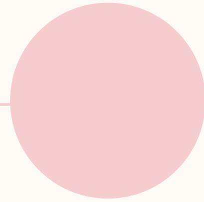
In adolescents admitted to Children's Hospital Los Angeles for severe anemia (Hgb≤8g/dL) secondary to acute heavy menstrual bleeding, does the addition of IV-CEE to high-dose COC's shorten length of hospital stay?

SUMMARY: WHICH MEDICATION DO I CHOOSE?



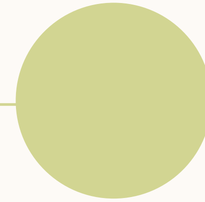
OUTPATIENT CHRONIC

- Progestins (PO or IM)
- Combined contraceptives (PO, patch, vaginal)
- 52mg LNG-IUD
- Tranexamic acid
- NSAIDs



OUTPATIENT ACUTE

- High-dose oral progestin taper
- High-dose COC taper
- Tranexamic acid
- +/-NSAIDs



INPATIENT ACUTE

- High-dose COC taper
- High-dose oral progestin taper
- IV-CEE + progestin or COC taper

WHEN TO REFER

Any abnormal uterine bleeding

9 periods per year is generally normal

Review a cycle calendar

…Email or call me!

1. Committee Opinion No. 651: Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign. *Obstet Gynecol.* 2015;126(6):1328.

2. Welt, C. (2021) Physiology of the normal Menstrual Cycle. *UpToDate*. Retrieved August 25, 2021, from https://www.uptodate.com/contents/physiology-of-the-normal-menstrual-cycle?search=normal%20menstrual%20cycle&usage_type=default&source=search_result&selectedTitle=2~150&display_rank=2

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5. Committee Opinion No. 128: Diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol.* 2012.

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13. Bryant-Smith AC, Lethaby A, Farquhar C, Hickey M. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD000249. DOI: 10.1002/14651858.CD000249.pub2

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15. James, AH. Diagnosis and management of women with bleeding disorders - international guidelines and consensus from an international expert panel. *Haemophilia*. 2011;17:3-5. doi:10.1111/j.1365-2516.2011.02557.x

PRACTICE CONTACT INFORMATION

Adolescent Medicine

CHOC Health Center, Centrum
1120 W. La Veta Ave., Suite 125
Orange, CA 92868
Scheduling: 888-770-2462
Fax: 855-246-2329

Specialty Care Physician Concierge Service
Phone: 714-509-4013

Physicians available via pingmd ®

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THANK YOU!

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mkhalighi@choc.org