

# **When Aunt Flo Comes to Town:** **Typical versus Atypical Menstruation and the** **Approach to Adolescents with Menstrual Concerns**

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# Disclosures

- None

# Objectives

- Review the menstrual cycle and typical menstruation
- Discuss causes and diagnosis of menstrual dysfunction in adolescents
- Outline first steps for treatment of menstrual dysfunction in adolescents
- Outline when and to whom to refer patients with menstrual dysfunction

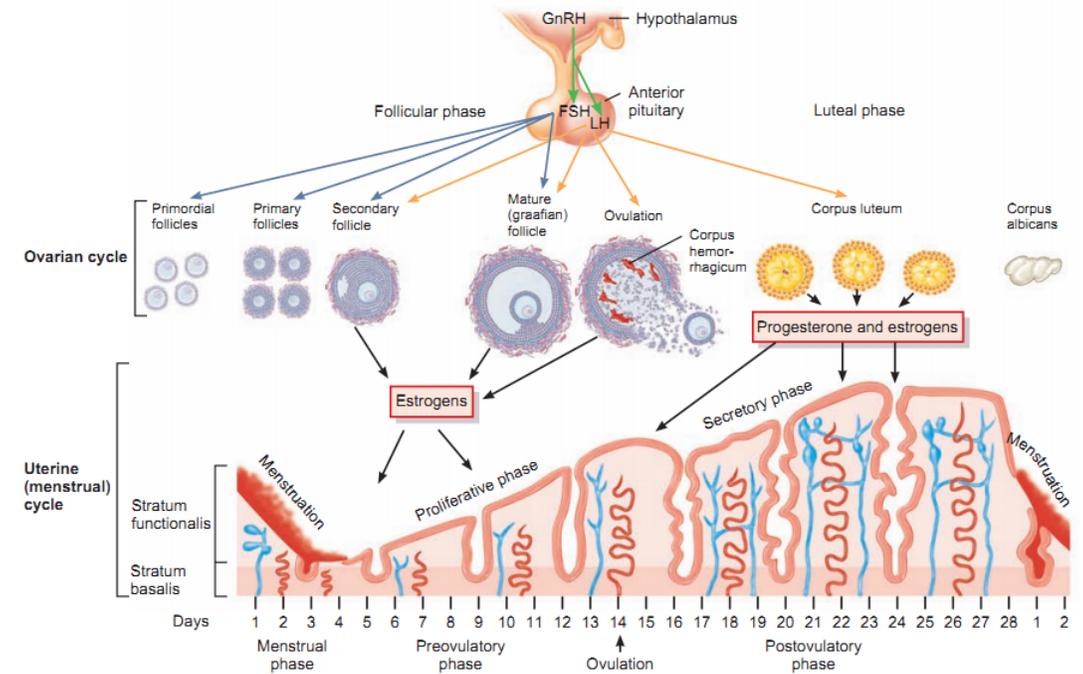
# Menstrual Cycle

Ovarian cycle has two phases

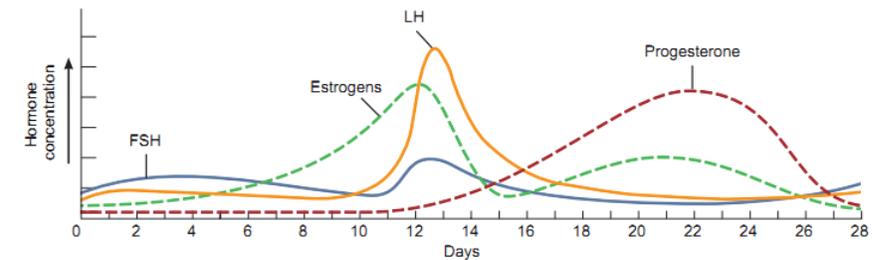
- **Follicular phase**
- **Luteal phase**

Uterine cycle has two phases

- **Proliferative phase**
- **Secretory phase**



(a) Hormonal regulation of changes in the ovary and uterus

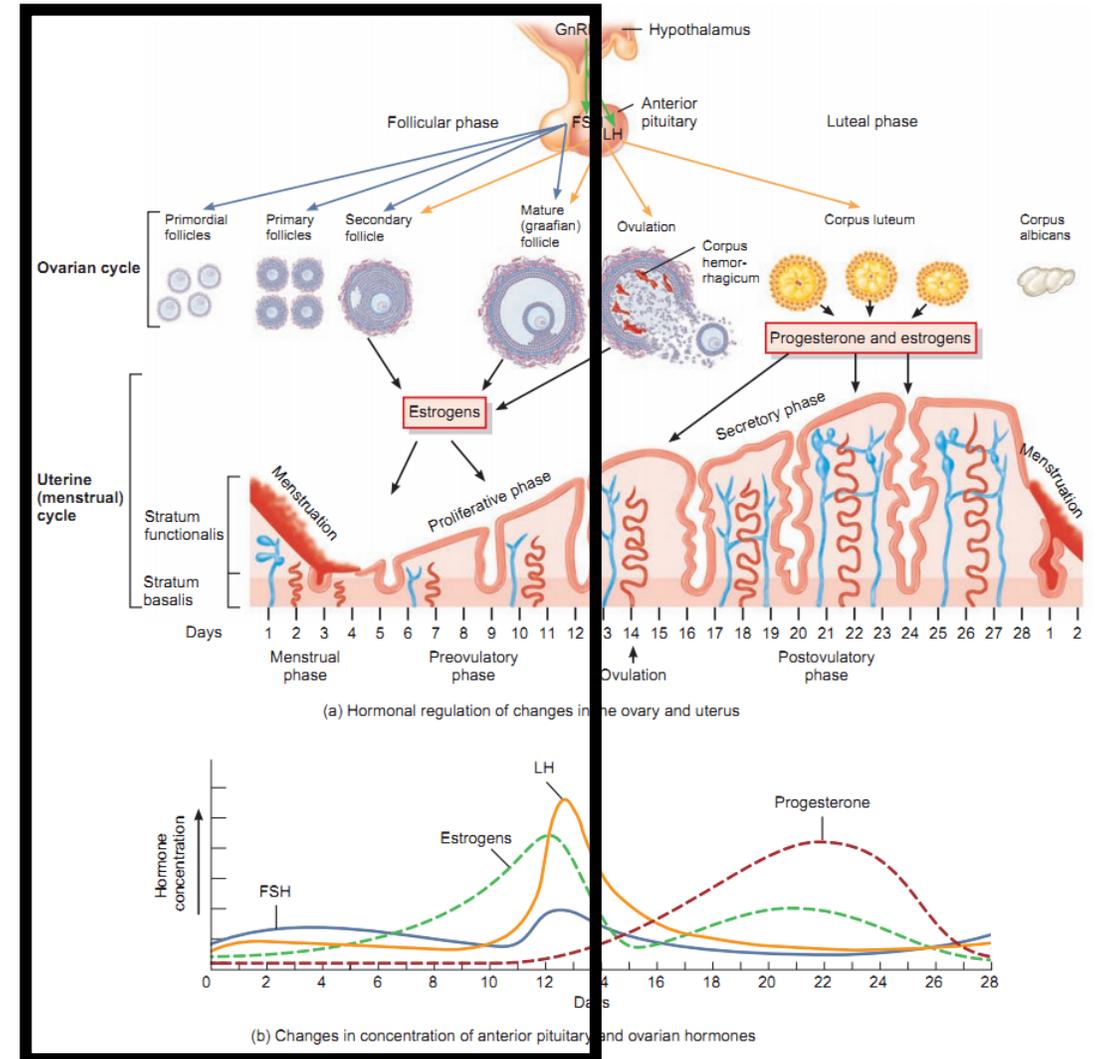


(b) Changes in concentration of anterior pituitary and ovarian hormones

# Menstrual Cycle

Follicular and proliferative phase

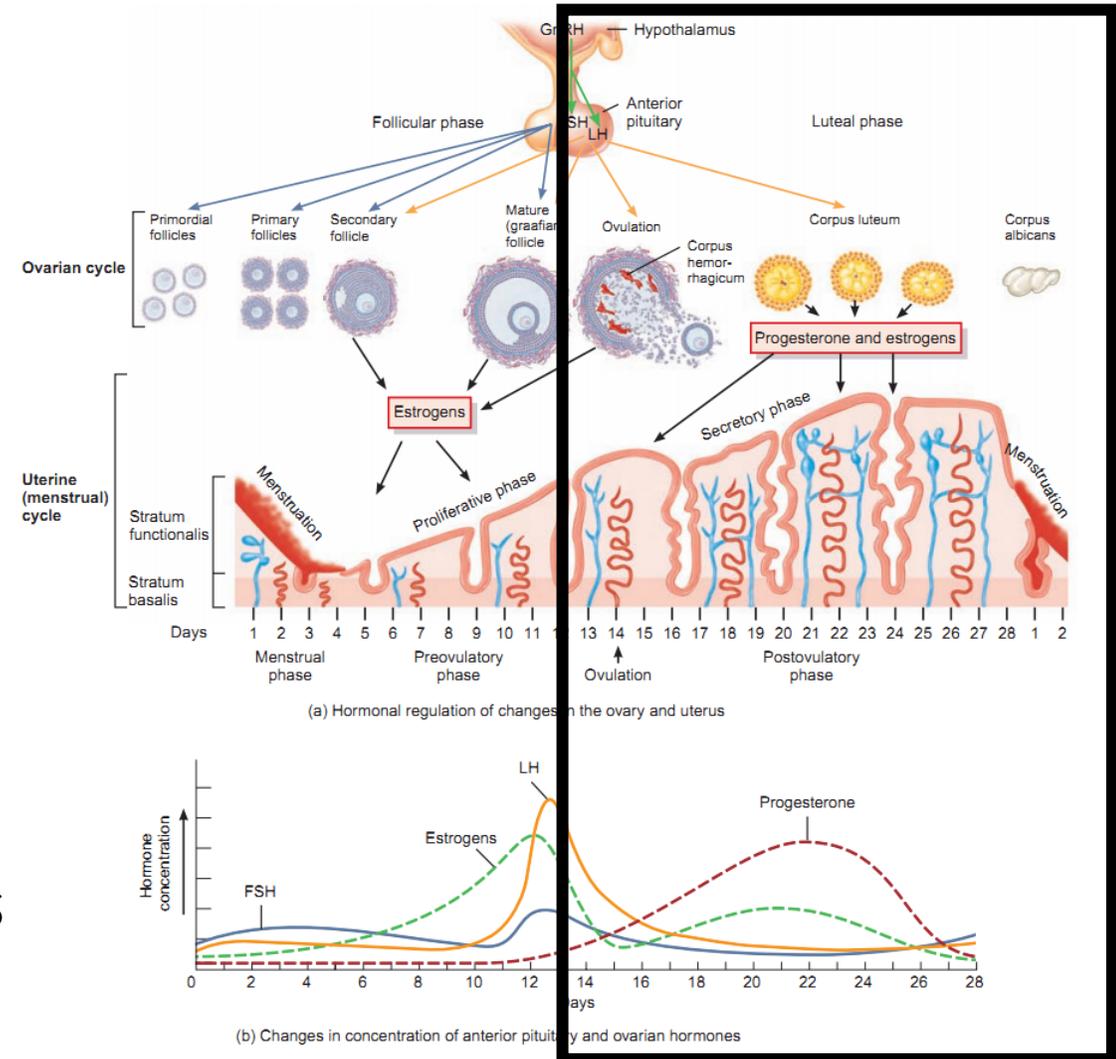
- FSH increases → follicles grow → **estradiol increases**
  - Feedback loop to hypothalamus leads to slight decrease in FSH
    - One follicle that is most sensitive to FSH becomes dominant follicle
  - LH surge → ovulation
  - Endometrium proliferates



# Menstrual Cycle

Luteal and secretory phase

- Corpus luteum forms at ovulation site → **produces progesterone**
  - Endometrium receptive to implantation
- Without pregnancy, corpus luteum undergoes atresia → **progesterone decreases**
  - Endometrial lining sheds = menses
  - Negative feedback decreases → FSH rises → new cycle



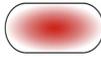
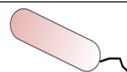
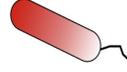
# What is typical?

- Age
  - Menarche: average 12.43 years
  - Abnormal: before age 8 or after age 15
- Interval: 21-45 days (average 28)
  - Can vary every month!
  - Varies more in adolescence and approaching menopause
- Duration: 2-7 days (average 5)
- Volume: < 80cc (average 35cc)
  - Abnormal: product changes < every 2 hours for more than 4 hours

# What is atypical?

**Abnormal uterine bleeding (AUB)** = any bleeding that is not “typical”

- Menorrhagia: prolonged, heavy bleeding
  - < 2 hours per product
  - > 7 days
  - Associated with iron-deficiency anemia
- Metrorrhagia: intermenstrual or irregular bleeding
  - Non-cyclic
  - Intermenstrual spotting, post-coital spotting
- Oligomenorrhea: cycles > 45 days and < 6 months
- Amenorrhea: no bleeding > 6 months

PADS	DAY							
	1	2	3	4	5	6	7	8
								
								
								
TAMPONS	DAY							
	1	2	3	4	5	6	7	8
								
								
								

# What causes menstrual dysfunction?

## Polyps

- Endometrial
- Endocervical

## Adenomyosis

## Leiomyoma

- Submucosal component

## Malignancy or hyperplasia

Structural

## Coagulopathies

- Inherited
- Acquired

## Ovulatory dysfunction

## Endometrial

- Infectious

## Iatrogenic

- Medication-induced: paragard, depo-provera, tamoxifen

## Not yet classified

Non-structural

# What causes menstrual dysfunction in adolescents?

## Polyps

- Endometrial
- Endocervical

## Adenomyosis

## Leiomyoma

- Submucosal component

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# Ovulatory dysfunction

## Immature HPO axis

- Up to 85% of all cycles within the first year of menarche are anovulatory
  - No ovulation → no corpus luteum → no progesterone rise and fall → no uniform endometrial shedding
    - Bleeding will be intermittent, irregular and can be prolonged
- Irregular menstrual cycles are considered “typical” within the first 1-3 years after menarche
  - Earlier menarche = earlier ovulatory pattern

# Ovulatory dysfunction

## Hyperandrogenism

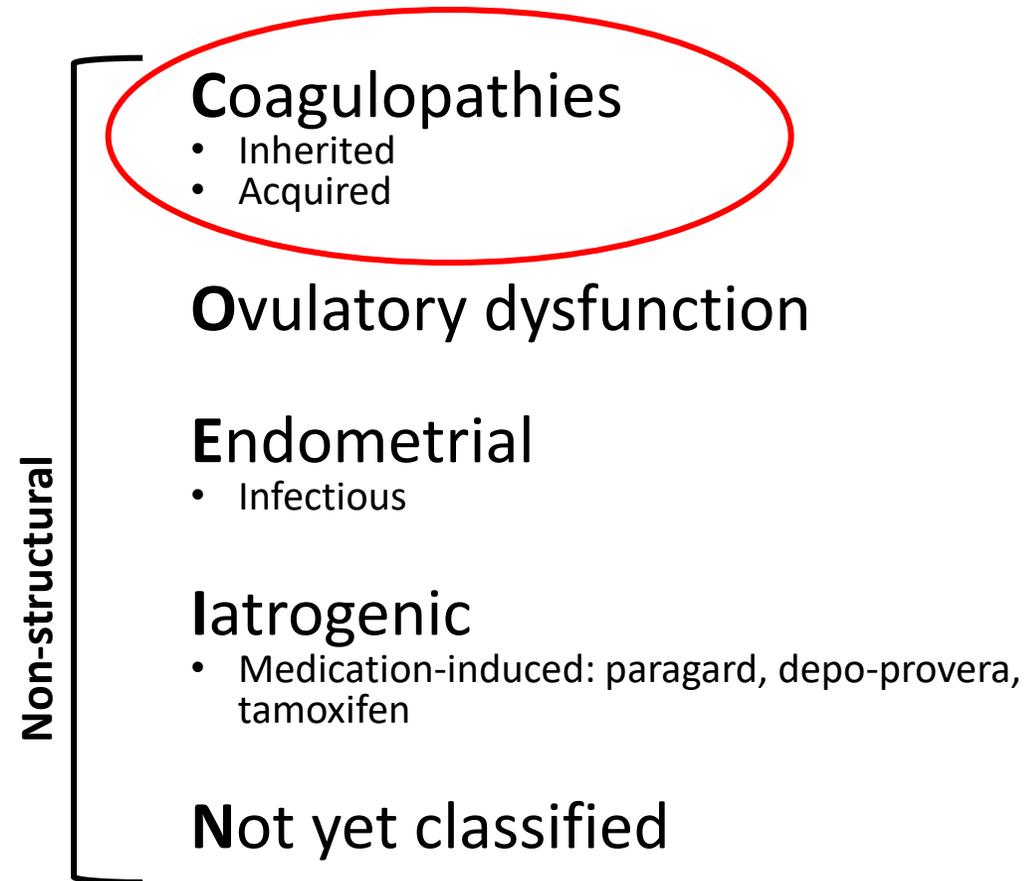
- Elevation in testosterone and adrenal androgens → LH/FSH dysregulation → impaired follicle maturation → anovulation → dysregulation uterine bleeding
  - Hormonal dysregulation contributes to additional systemic side effects:
    - Acne
    - Hirsutism
    - Insulin resistance
- Most common endocrinopathy in premenopausal women
  - Persistent and pathologic prevalence in adolescence is unclear
    - Fluctuation in androgen production is common in adolescence
    - Most adolescents with irregular menses and elevated androgens are considered “at risk” for PCOS
      - Defer diagnosis for at least 2 years from menarche

# Ovulatory dysfunction

## Hypothalamic amenorrhea

- Hypothalamic response to stress and negative energy balance → suppressed and dysregulated pulseatility of gonadotropins → low estradiol → no LH surge + lack of proliferation of endometrial lining → amenorrhea
  - Spectrum: mild disturbances in endocrine function to severe estrogen deficiency
  - Lab abnormalities are typically subtle unless hypothalamic dysfunction is severe

# What causes menstrual dysfunction in adolescents?



# Coagulopathies

## Bleeding Disorders

- Lack of clotting factors necessary to stop bleeding → heavy and prolonged bleeding episodes
- 50% of girls with bleeding disorders present at menarche with heavy menstrual bleeding
  - Von Willebrand disease
  - Also: platelet function defects, thrombocytopenia, and clotting factor deficiencies
- Who needs screened?
  - Heavy menstrual bleeding since menarche
  - **One** of the following: postpartum hemorrhage, excess bleeding with surgery, bleeding with dental work
  - **Two** or more of the following: bruising, epistaxis, frequent gum bleeds, family history of bleeding symptoms

# Evaluation

- Clinical history and lab evaluation are most valuable for evaluation of AUB in adolescents
- Some tools used in the workup of AUB in adults are **rarely indicated** with the initial evaluation of AUB **in adolescents**
  - Internal pelvic exam
  - Pelvic ultrasound



# Evaluation

## Irregular bleeding

- LH/FSH/estradiol
- Free and total testosterone
- DHEA-S
- 17-OHP
- TSH
- Prolactin
- bHCG

### Order for:

- >3-6 months between periods or no period for 3-6 months
- Persistent irregularity 3 years after menarche
- New irregularity at any age

# Evaluation

## Heavy bleeding

- CBC
- Iron studies
- Von Willebrand panel (factor VIII activity, vWB antigen, vWB activity/ristocetin cofactor)
- PT/PTT

### Order for:

- Any signs or symptoms of anemia or iron deficiency
- Overflow accidents with every period or routine bleeding >1 product q2hours

\* Evaluation for bleeding disorder may be altered by current bleeding and exogenous estrogens

# What happens when the work-up is normal?

- **Normal labs are the most common outcome** when testing for abnormal uterine bleeding in adolescents
  - For heavy bleeding, most likely normal variant
  - For irregular bleeding, most likely immature HPO axis
    - Fluctuations in sleep, stress, diet, and growth contribute to anovulation
    - Up to 50% of cycles will be anovulatory 4 years after menarche
  - For amenorrhea, rule out eating disorders, RED-S, and premature ovarian insufficiency
    - Repeat FSH/LH/estradiol 1 month after initial assessment
    - DXA for evaluation of bone mineral density if amenorrhea >6 months

# Treatment algorithm

## Irregular bleeding

- Criteria for treatment (any 1):
  - Desire for menstrual regulation
  - Anemia secondary to prolonged bleeding
  - >5 years of menstrual irregularity

### PERIOD Tracker<sup>™</sup>

	J	F	M	A	M	J	J	A	S	O	N	D
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2										•	•	
3	•									•		
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# Treatment algorithm

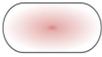
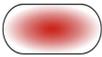
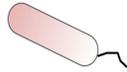
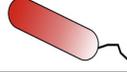
## Irregular bleeding

- Treatment goal: menstrual regularity
  - Combined estrogen-progesterone pills/patches/ring used cyclically
    - Cryselle (0.3mg norgestrel/0.03mg ethinyl estradiol)
    - Sprintec (0.25mg norgestimate/0.035mg ethinyl estradiol)
    - Xulane (0.150mg norelgestromin/0.035mg ethinyl estradiol) transdermal
  - PRN progesterone x10 days q month or q2months
    - Medroxyprogesterone acetate (provera) 10mg

# Treatment algorithm

## Heavy or prolonged bleeding

- Criteria for treatment (any 1):
  - Desire for improvement in menses
  - Anemia, iron deficiency, or history of blood transfusion after menarche
  - Known bleeding disorder

PADS	DAY							
	1	2	3	4	5	6	7	8
								2
					2		1	
	4	2						
TAMPONS	DAY							
	1	2	3	4	5	6	7	8
						1	1	
			2	2	3	3		
	7	7	4	3				

# Treatment algorithm

## Heavy or prolonged bleeding

- Treatment goal: menstrual suppression
  - Combined estrogen-progesterone pills/patches/ring used cyclically or continuously
    - Continuous preferred for complete menstrual suppression
      - If breakthrough bleeding, stop medications for 4 days and then restart
    - COC taper only with heavy to prevent hospitalization
  - Progestin-only options
    - Norethindrone acetate (aygestin) 5-15mg daily
    - Depo-provera q10-12 weeks
    - Levonorgestrel (mirena) IUD

# Treatment algorithm

## Non-hormonal options for menstrual manipulation

- NSAIDs: 400-800mg ibuprofen q8hours throughout menses
  - Less blood loss than placebo
  - Do not decrease duration of menses
  - Less effective than antifibrinolytic or hormonal therapies
- Tranexamic acid (TXA): 1300mg TID x 5 days starting on the first day of menses
  - 40% reduction in blood loss
  - Minimal data in patients with increased risk of VTE; overall thought to be safe

# Referral

- Adolescent medicine, pediatric gynecology, and adult ob/gyn all have the knowledge and tools to treat AUB in adolescents
  - Some patients may benefit from multi-disciplinary approach
    - Menstrual-related anemia → heme/gyn
      - At CNMC call 202-476-7060 to schedule
    - Metabolic syndrome + menstrual irregularity → endo/gyn
      - At CNMC call 202-476-3440 to schedule
- Any patient with a complex medical history or bleeding refractory to initial treatment should be seen by a pediatric gynecologist
  - CNMC clinic scheduling: 202-476-2150
    - CNMC PAG nurse: 202-476-5218, [PAG@cnmc.org](mailto:PAG@cnmc.org)
  - PSV clinic scheduling: 703-876-2788
    - PSV PAG nurse: 703-635-2164, [PSVGYN@psvcare.org](mailto:PSVGYN@psvcare.org)

*Thank you!*

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