

Abnormal Uterine Bleeding: Just a part of life?

Tanya M. Evers, MD, MEd, FACOG
Faculty-Obstetrics and Gynecology
Family Medicine Residency Program
Tallahassee Memorial HealthCare
Tallahassee, FL

Disclosure statement

- ▶ I have no disclosures or conflicts of interest to report.

Prepubertal Bleeding

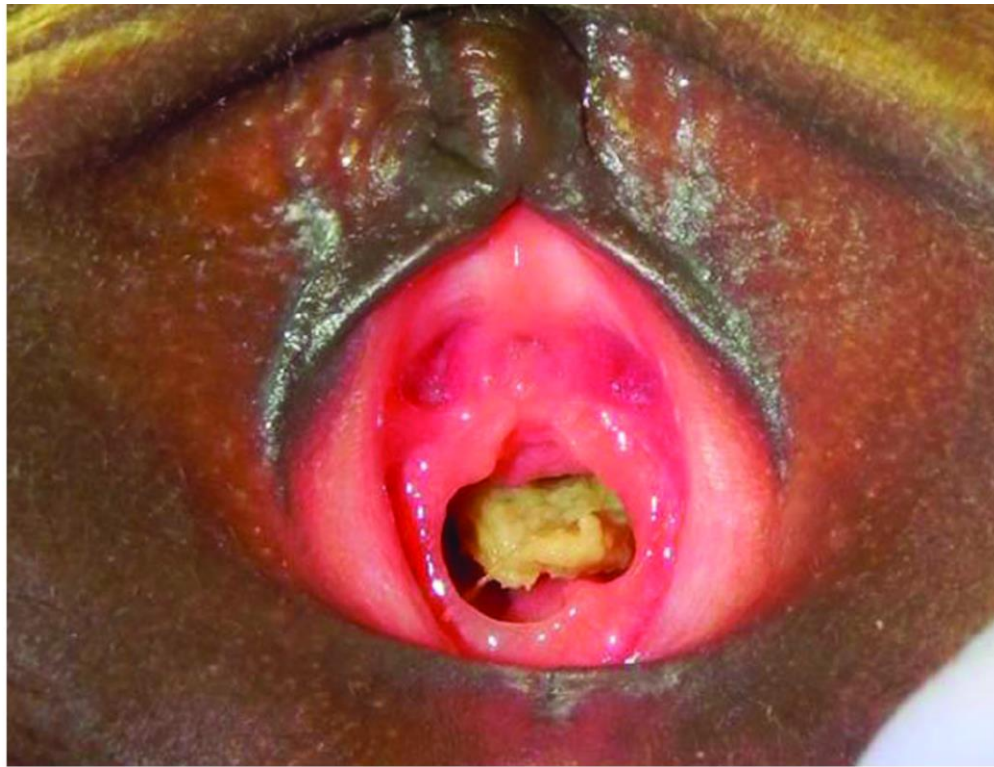
- ▶ Foreign body
- ▶ Tumors
- ▶ Urethral prolapse
- ▶ Lichen sclerosis
- ▶ Vulvovaginitis
- ▶ Condyloma acuminata
- ▶ Trauma
- ▶ Precocious puberty
- ▶ Exogenous hormone use

Vaginal bleeding in prepubertal girls

Table 3
Etiology of Vaginal Bleeding (n = 86)

Etiology	Patients, n	Patients, %
Local lesion	47	54.7
Trauma	39	45.3
Vulvovaginitis	5	5.8
Vaginal tumor	1	1.2
Lichen sclerosis	1	1.2
Vulvar papilloma	1	1.2
Hormonal	16	18.6
Hormonal withdrawal bleeding	9	10.5
Precocious puberty	6	7.0
Ovarian tumor	1	1.2
Unknown	23	26.7
All	86	100

Foreign body



Source: Barbara L. Hoffman, John O. Schorge, Karen D. Bradshaw, Lisa M. Halvorson, Joseph I. Schaffer, Marlene M. Corton: *Williams Gynecology*, 3rd Edition: www.accessmedicine.com
Copyright © McGraw-Hill Education. All rights reserved.

Abnormal Uterine Bleeding: Reproductive Age

- ▶ Pregnancy
 - ▶ Intrauterine→Mole→Ectopic
- ▶ Structural
 - ▶ Congenital outflow obstruction→Cancers along the tract
- ▶ Anovulation
 - ▶ HPO axis→Thyroid→Prolactin→Androgens
- ▶ Exogenous
 - ▶ Meds→IUD/Foreign Body→Trauma
- ▶ Infection
 - ▶ STDs→Endometritis
- ▶ Systemic
 - ▶ Coagulopathies

This is...

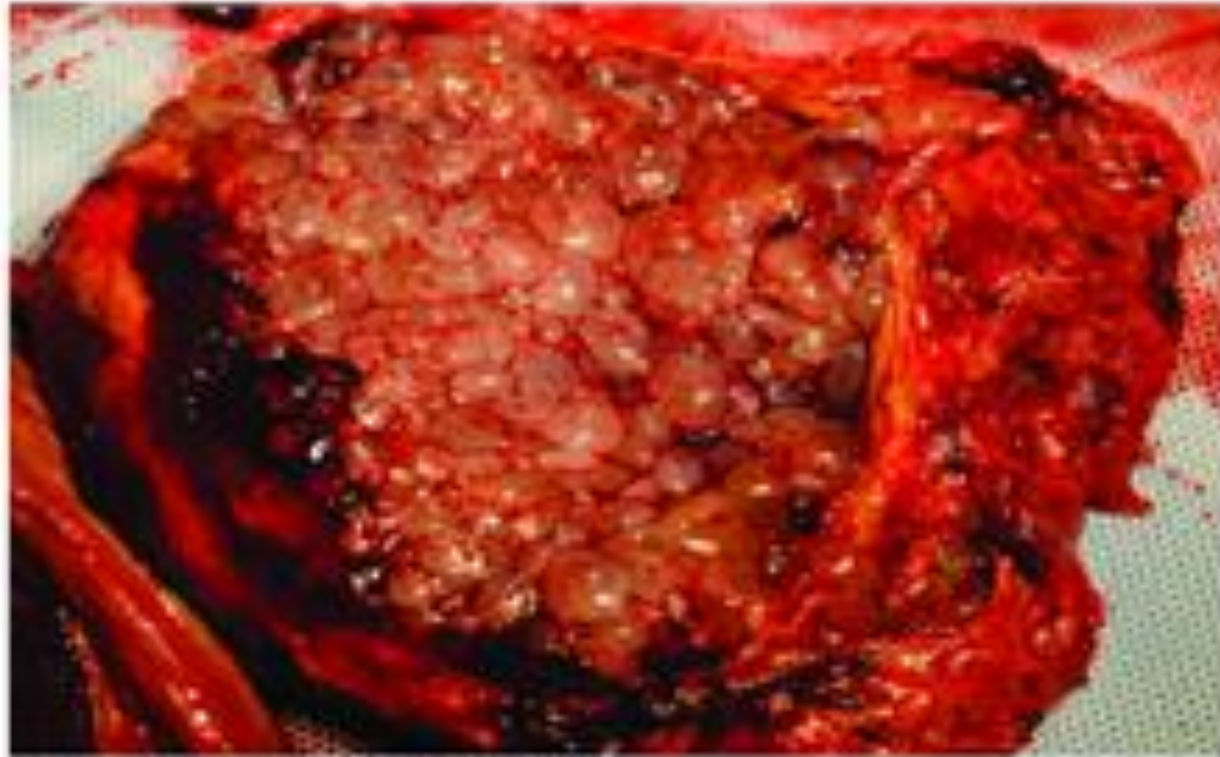


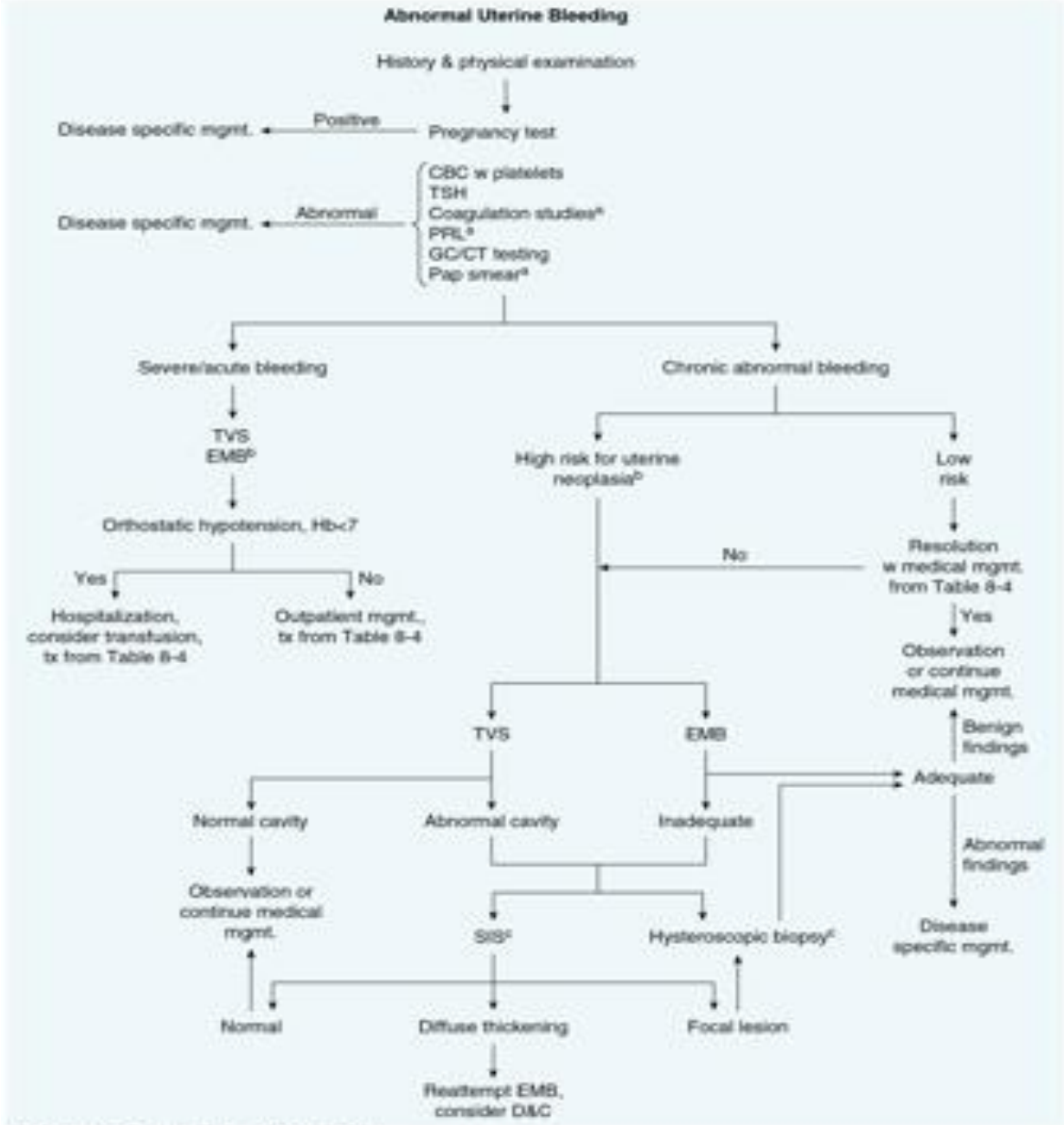
Figure 1. Gross pathology specimen of a large, lobulated, reddish-brown mass, likely a tumor, surrounded by a layer of reddish-brown tissue, possibly the capsule or surrounding tissue. The overall color is a deep red, suggesting a high degree of vascularity or hemorrhage.

Hoffman et al.
GTD

Abnormal Uterine Bleeding: Reproductive age

- ▶ Rule out:
 - ▶ Pregnancy
 - ▶ Cancer

Algorithm: AUB



Source: Hoffman et al., Hoffmann, et al. © 2010 American College of Obstetricians and Gynecologists, Inc. All rights reserved. www.acog.org

ACOG Classification

- ▶ PALM-COEIN
 - ▶ Structural
 - ▶ Polyp
 - ▶ Adenomyosis
 - ▶ Leiomyoma (Submucosal and “other”)
 - ▶ Malignancy and Hyperplasia
 - ▶ Non-structural
 - ▶ Coagulopathy
 - ▶ Ovulatory dysfunction
 - ▶ Endometrial
 - ▶ Iatrogenic
 - ▶ Not yet classified

Endometrial Evaluation

- ▶ EM Cancer >35yo
 - ▶ Although not impossible if <35 yo
 - ▶ Biopsy if risk factors
- ▶ Goal of EM evaluation
 - ▶ Rule out cancer
 - ▶ Direct therapy if not cancer
 - ▶ Ex: Anovulatory cycles vs polyps
- ▶ Global vs focal processes of the uterus
 - ▶ Pipelle (blind biopsy)—global processes
 - ▶ EM cancer often focal in nature

Ultrasound Use

- ▶ TVUS
 - ▶ Timing
 - ▶ If cycling: immediately after monthly menses ends
 - ▶ If Not cycling: anytime
 - ▶ Use in “triage”
 - ▶ Anatomic pathology-If No...
 - ▶ Dysfunctional anovulatory bleeding (cycling)
 - ▶ Atrophy (PMP)
 - ▶ Global process (Okay to perform blind biopsy ie pipelle)
Vs
 - ▶ Focal abnormality (requires H/S to visualize/sample)
 - ▶ 4mm or less in PMP
 - ▶ Almost 99.4-100% NPV
 - ▶ Incidental EM thickening in PMP
 - ▶ 10-17%
 - ▶ No need to sample unless risk factors

Endometrial “Stripe”

Table 2. Prospective Trials of Endometrial Thickness and Cancer Findings in Postmenopausal Women With Bleeding

Study	Endometrial Thickness (mm)*	Number of Women	Number of Cancers	Negative Predictive Value (%)
Karlsson et al, 1995 ²⁰	4 or less	1,168	0	100
Ferrazzi et al, 1996 ²¹	4 or less	930	2	99.8
	5 or less		4	99.6
Gull et al, 2000 ²²	4 or less	163	1	99.4
Epstein and Valentin, 2001 ²³	5 or less	97	0	100
Gull et al, 2003 ²⁴	4 or less	394	0	100

*Determined by transvaginal ultrasonography.

Reprinted from The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. ACOG Committee Opinion No. 440. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 114:409-11.

US based triage with AUB

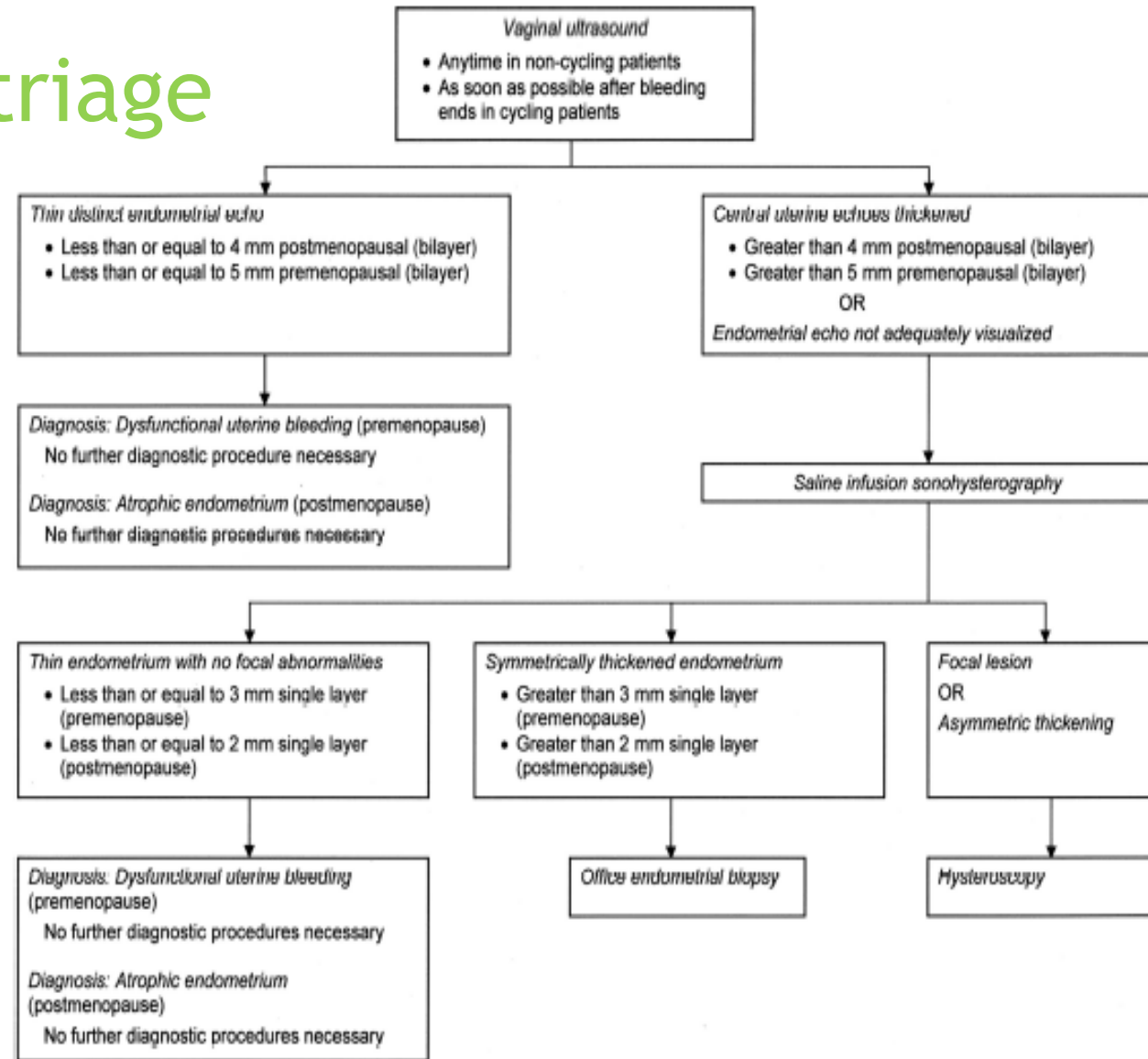


Fig. 7. Ultrasonography-based triage for patients with abnormal uterine bleeding.
Goldstein. *Modern Evaluation of the Endometrium*. Obstet Gynecol 2010.

Meta-analysis urged tighter guideline

- ▶ Used individual patient data instead of reported data
- ▶ Found $\leq 3\text{mm}$ on TVUS in PMB 98% sensitivity
 - ▶ Vs 95% $\leq 4\text{mm}$ (and 90% $\leq 5\text{mm}$)

Endometrial Hyperplasia



Hoffman et al.
EMCa

WHO classifications of hyperplasia 1994

TABLE 33-2 World Health Organization Classification of Endometrial Hyperplasia

Types	Progressing to Cancer (%)
Simple hyperplasia	1
Complex hyperplasia	3
Simple atypical hyperplasia	8
Complex atypical hyperplasia	29

Data from Kurman RJ, Kaminski PF, Norris HJ: The behavior of endometrial hyperplasia. A long-term study of "untreated" hyperplasia in 170 patients. *Cancer* 1985 Jul 15;58(2):403-412.

Date of download: 11/16/16 from AccessMedicine: accessmedicine.mhmedical.com, Copyright© McGraw-Hill Education. All rights reserved.

Newer method of classification

- ▶ EIN: Endometrial Intraepithelial Neoplasia
- ▶ Two categories of hyperplasia
 - ▶ Normal endometria diffusely responding to hormones
 - ▶ Focal proliferative lesions; increase risk of EM cancer
- ▶ System more accurate and reproducible
- ▶ Categorizing based on:
 - ▶ Glandular volume
 - ▶ Architectural complexity
 - ▶ Cytologic abnormality

Endometrial Cancer



SAG ENDOMETRIUM
100.00cm 100.00cm 100.00cm 100.00cm
100.00cm 100.00cm 100.00cm 100.00cm
100.00cm 100.00cm 100.00cm 100.00cm

Hoffman et al.
EMCa

Pipelle vs Curette

- ▶ Randomized control study to compare pipelle to a curette device for office EM sampling
- ▶ Same pain scores for both
- ▶ Most patients were of reproductive age
- ▶ Does that make a difference in perception?

A prospective cohort study

- ▶ First PMB → TVUS EMS >4mm → Benign EMBx
- ▶ Time until next bleed (median 49 weeks)
- ▶ Recurrence rate 20%
- ▶ Method of acquiring initial bx did not affect timing or outcome of further bleeding
- ▶ Sample at next bleed

Global “Fat Scale”

- ▶ <http://www.bbc.com/news/health-18770328>

Does a negative EMBx predict future risk?

- ▶ Nested case control study
- ▶ EM CA after benign biopsy/D&C
 - ▶ About 25% of the women in the study with CA had previous benign biopsy
 - ▶ Median time to CA 6.7years
 - ▶ If reason to biopsy, already have risk factors
 - ▶ Ex: obesity, no history of OCP use, history of EM polyp, non-polyposis colorectal cancer related malignancy
 - ▶ Possible interventions include regular screenings, OCP use, weight loss, elective (ppx) hysterectomy
 - ▶ Requires additional studies for cost effectiveness

Why not perform surgery for EMCa?

- ▶ Desire future fertility
- ▶ Tx with progestins
 - ▶ Systemic (Megestrol, Medroxyprogesterone, OCPs)
 - ▶ Local (Levonorgestrel IUD)
 - ▶ Q 3 month bx
 - ▶ 42% still with stable/persistent disease @ 12 months s/p treatment
 - ▶ Vigilance is key

Progestin therapy

- ▶ Dose, scheduled, duration, route have not been standardized

Table 6. Hormonal Treatment for Atypical Endometrial Hyperplasia or Endometrial Intraepithelial Neoplasia

Treatment	Dosage or Length
Medroxyprogesterone acetate	10–20 mg daily or cyclic 12–14 d/mo
Depot medroxyprogesterone	150 mg intramuscularly every 3 mo
Micronized vaginal progesterone	100–200 mg daily or cyclic 12–14 d/mo
Megestrol acetate	40–200 mg per d, usually reserved for women with atypical hyperplasia
Levonorgestrel-containing intrauterine device	1–5 y

References

BBC News Health. Where are you on the global fat scale? <http://www.bbc.com/news/health-18770328>. Retrieved 11.16.16.

Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2012; 120: 197-206.

Goldstein, S. Modern evaluation of the endometrium. *Obstetrics and Gynecology*. 2010, July; 116 (1): 168-176.

Hoffman, Barbara L., et al.. "Abnormal Uterine Bleeding." *Williams Gynecology, 3e*. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Hoffman B.L., Schorge J.O., Bradshaw K.D., Halvorson L.M., Schaffer J.I., Corton M.M. Eds. Barbara L. Hoffman, et al. New York, NY: McGraw-Hill, 2016, <http://accessmedicine.mhmedical.com.proxy.lib.fsu.edu/content.aspx?bookid=1758&Sectionid=118168196>.

Hoffman, Barbara L., et al.. "Endometrial Cancer." *Williams Gynecology, 3e*. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Hoffman B.L., Schorge J.O., Bradshaw K.D., Halvorson L.M., Schaffer J.I., Corton M.M. Eds. Barbara L. Hoffman, et al. New York, NY: McGraw-Hill, 2016, <http://accessmedicine.mhmedical.com.proxy.lib.fsu.edu/content.aspx?bookid=1758&Sectionid=118172898>.

Hoffman, Barbara L., et al.. "Gestational Trophoblastic Disease." *Williams Gynecology, 3e*. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Hoffman B.L., Schorge J.O., Bradshaw K.D., Halvorson L.M., Schaffer J.I., Corton M.M. Eds. Barbara L. Hoffman, et al. New York, NY: McGraw-Hill, 2016, <http://accessmedicine.mhmedical.com.proxy.lib.fsu.edu/content.aspx?bookid=1758&Sectionid=118173613>.

Hoffman, Barbara L., et al.. "Pediatric Gynecology." *Williams Gynecology, 3e*. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Hoffman B.L., Schorge J.O., Bradshaw K.D., Halvorson L.M., Schaffer J.I., Corton M.M. Eds. Barbara L. Hoffman, et al. New York, NY: McGraw-Hill, 2016, <http://accessmedicine.mhmedical.com.proxy.lib.fsu.edu/content.aspx?bookid=1758&Sectionid=118169397>.

Hubbs, JL et al. Systemic and local hormone therapy for endometrial hyperplasia and early adenocarcinoma. *Obstetrics and Gynecology*. *Obstetrics and Gynecology*. 2013, June; 121 (6):1172-1180.

Leclair, CM et al. Pain experienced using two different methods of endometrial biopsy: A randomized controlled trial. *Obstetrics and Gynecology*. 2011, March; 117 (3):636-641.

Soderstrom H.F. et al. Vaginal bleeding in prepubertal girls: etiology and clinical management, *J Pediatr Adolesc Gynecol* 29 (2016) 280-285.

The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. ACOG committee opinion No. 440. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 114: 409-11.

Timmermans, A et al. Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: A systematic review and meta-analysis. *Obstetrics and Gynecology*. 2010, July; 116 (1):160-167.

Timmermans et al. Follow up of women after a first episode of postmenopausal bleeding and endometrial thickness greater than 4 millimeters. *Obstetrics and Gynecology*. 2008, Jan; 111 (1): 137-143.

Torres, ML et al. Risk factors for developing endometrial cancer after benign endometrial sampling. *Obstetrics and Gynecology*. 2012, Nov; 120 (5): 998-1004.

Trimble, C.L. et al. Management of endometrial precancers. *Obstetrics and Gynecology*. 2012, Nov; 120 (5): 1160-1175.