Contraceptive Options for Patients with Risk or History of Thrombosis

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OPA Annual Conference & Trade Show
April 5-7, 2024

OHIO PHARMACISTS ASSOCIATION

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Disclosure Statement

- The presenter has no relevant financial relationship(s) with ineligible companies to disclose.

  and

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

Learning Objectives

At the completion of this activity, the participant will be able to:

1. Explain the risk of combined oral contraception in patients with risk or history of thrombosis
2. Recall options for contraception for patients with risk of thrombosis
3. Examine options for contraception for patients with history of thrombosis currently on anticoagulation
4. Discuss upcoming OTC contraception options for patients and their risk of thrombosis

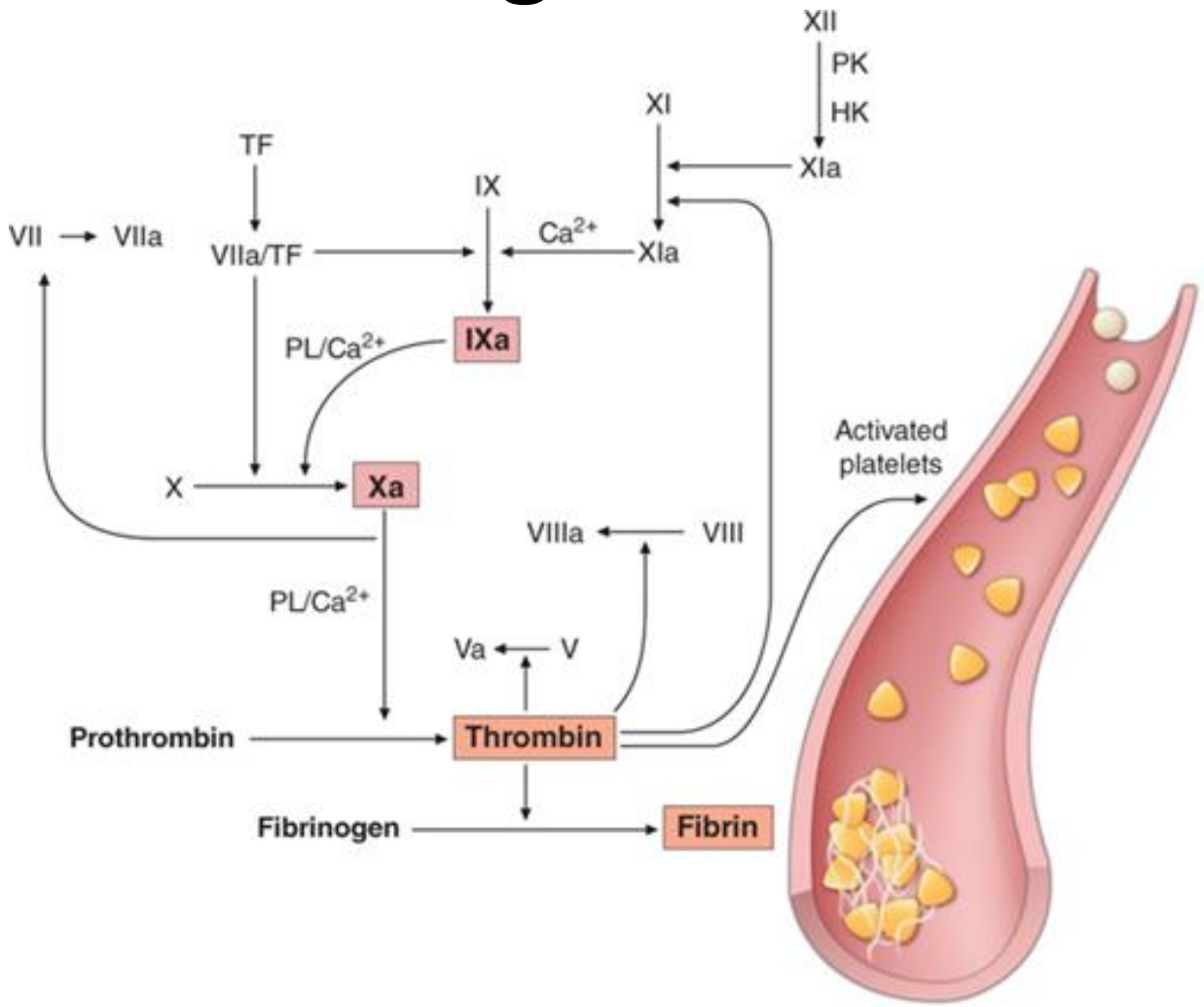
Prevalence

- 64.9% of women aged 15-49 reported contraceptive use from 2015-2017
  - 12.6% of these used oral contraception
  - 10.3% of these used long acting reversible contraception
- Up to 900,000 patients are affected by VTE/PE annually
  - Incidence of first DVT in the general population is 5 per 10,000 person-years
  - Similar in women and men when adjusting for factors related to reproduction and birth control
- Combined hormonal contraceptives (CHCs) increase VTE risk
  - 3-15/10,000 woman-years vs 1-5/10,000 woman-years in non-users

Risk Factors for Venous Thrombosis

- May be genetic or acquired
  - Immobilization/venous stasis
  - Genetic factors: factor V Leiden mutation, antithrombin deficiency, protein C or S deficiencies
  - Cancer
  - Increased age
  - Male sex
  - Infection
  - Renal disease
  - Weight loss
  - Pregnancy
  - Hormone replacement therapy / oral contraceptive use

Clotting Cascade



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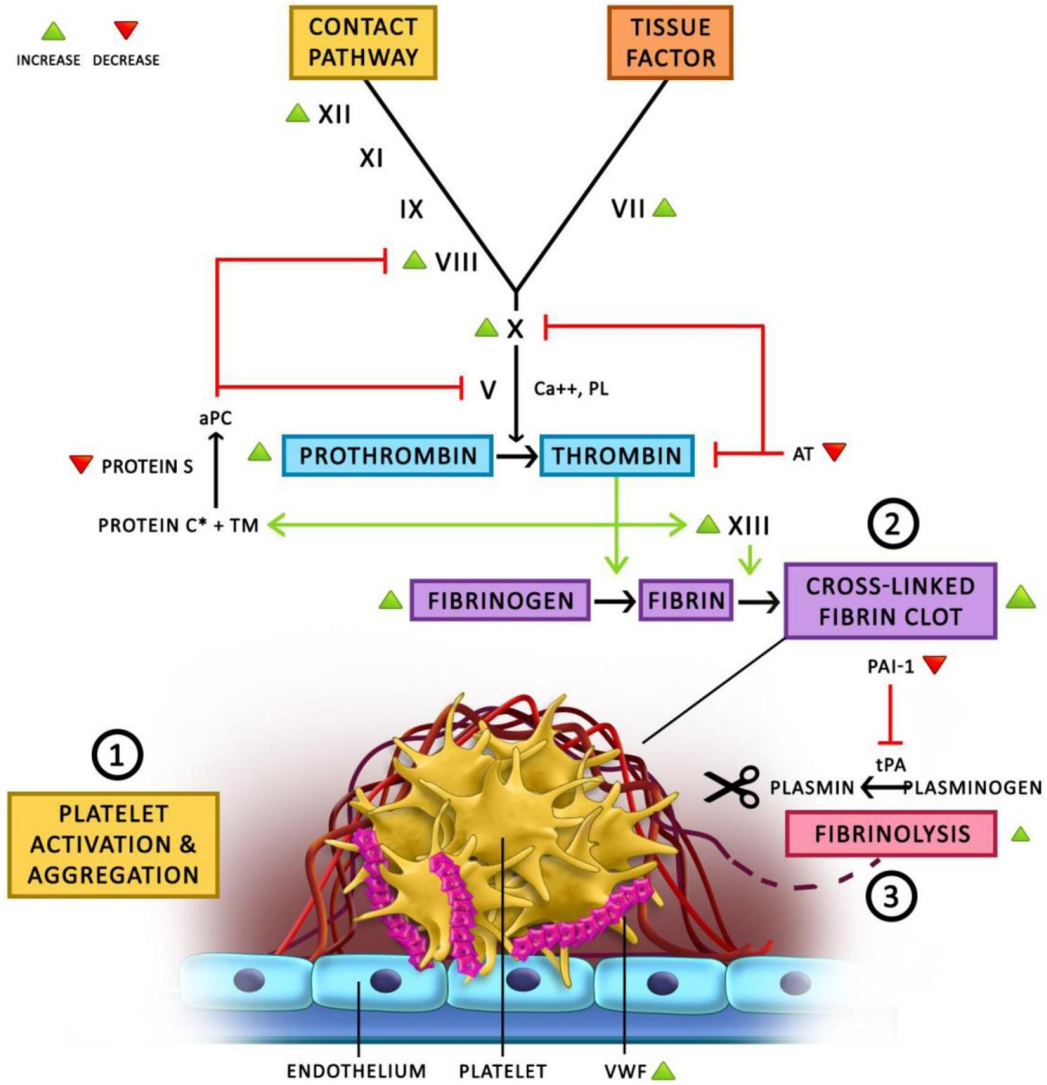
Thrombosis and Estrogen



Abou-Ismail MY, Citla Sridhar D, Nayak L. Estrogen and thrombosis: A bench to bedside review. Thromb Res. 2020 Aug;192:40-51. doi: 10.1016/j.thromres.2020.05.008. Epub 2020 May 11. PMID: 32450447; PMCID: PMC7341440.

Contraceptive Options

Hormonal [6]	**Non-Hormonal** [6]
Combined Oral Contraceptives (pills, patches, vaginal rings)	Sterilization (tubal ligation)
Progestin-only contraceptives (pills, IUD, subcutaneous implant, injections)	Copper IUD
	Spermicides
	Barrier methods (diaphragm, cervical cap, condoms)

Non-Hormonal Contraceptive Options

Contraception Type	Mechanism of Action	Considerations
Sterilization (tubal ligation)[7]	Fallopian tubes cut and tied to prevent sperm from reaching the egg	Surgical procedure May not be reversible
Copper IUD [8]	Not well defined May prevent sperm transport and fertilization or cause chemical changes toxic to sperm	Heavy menstrual bleeding Pelvic cramps Ectopic pregnancy Failure rate <1%
Spermicides (film, sponge, gel)[9]	Damages sperm cell membrane Physical barrier with some preparations	Application-site reaction Allergic contact dermatitis Urinary Tract Infection Failure rate 12-32%
Barrier methods [10] (diaphragm, cervical cap, condoms)	Physical barrier	Failure rate 12-32%

Hormonal Contraceptive Options

Hormonal Options[6]	
Combined Oral Contraceptives	Pills Patches Vaginal rings
Progestin-only contraceptives	Pills IUD Subcutaneous implant Injection

Hormonal contraceptives with anticoagulation

Table 2. Hormonal birth control methods – risk of venous thromboembolism (VTE) and effectiveness with typical use.[8,11–13]

Method	Risk of VTE with no anticoagulation	Risk of VTE with anticoagulation	Typical use effectiveness
Combined hormonal contraceptives			
• pills	Increased	Not increased	91%
• patches	Increased	Not increased	91%
• vaginal rings	Increased	Not increased	91%
Progestin-only contraceptives			
• pills	Not increased	Not increased	91%
• levonorgestrel IUD	Not increased	Not increased	99%
• subcutaneous implant	Not increased	Not increased	99%
• injections	Increased	Not increased	94%

https://journals.sagepub.com/doi/pdf/10.1177/1358863X17690601

Current guidance for patients on anticoagulation

- **Research and Practice in Thrombosis and Haemostasis:** [11]
  - Guidance for patients with heavy menstrual bleeding
  - May initiate levonorgestrel IUD, etonogestrel subdermal implant, or progestin-only pill
  - Combined oral contraception or injectable medroxyprogesterone* acetate may be continued or initiated if anticoagulation is continued
    - Recommend to discontinue estrogen therapy >1 month prior to discontinuing anticoagulation

Current guidance for patients on anticoagulation

- **Recurrent VTE & abnormal uterine bleeding** [12]
  - Evaluated recurrent VTE in 1,888 women <60 years of age with abnormal uterine bleeding with or without the use of hormonal therapy
  - Patients were anticoagulated with rivaroxaban, enoxaparin, or vitamin K agonists
  - 2016 Study found no increased risk of recurrent VTE in women with therapeutic anticoagulation (enoxaparin/VKA or rivaroxaban) that used hormonal contraception
  - Incidence of VTE was 3.7% versus 3.8% per year
    - Hazards ratio 0.56; 95% CI (0.23-1.39)
  - Concluded no increased risk of recurrent VTE in anticoagulated patients

Hormonal contraceptives without anticoagulation[6]

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• injections	Increased	Not increased	94%

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Current guidance for patients with risk/history of thrombosis

- Package insert contraindications to COCs include thromboembolic disorders or history of thrombosis [13]
- Progestin only contraception [6]
  - No increased VTE risk, with exception of progestin-only injection

Current guidance for patients with risk/history of thrombosis

- **American Society for Reproductive Medicine 2016 Guideline:** [4]
  - High dose oral contraception (>50 ug) associated with higher VTE risk
  - No evidence found that doses <35 ug further decreases VTE risk
  - Insufficient evidence that the patch or vaginal ring has a different risk than COCs
  - ***No recommendation in one type of preparation over another in terms of VTE risk***

Current guidance for patients with risk/history of thrombosis

- **American Society for Reproductive Medicine 2016 Guideline:** [4]
  - VTE risk may be higher with third/fourth generation progestins
    - Lack of high quality studies
    - Decision for type of COC should not be based on type of progestin

Recommendation: reasonable to use any available preparation should combined hormonal contraception be found appropriate

O-Pill

- Approved July 13, 2023[15]
- Previously available Rx only
- Exact release date unknown

Contraindications [16]	**Consult Healthcare Provider Prior to Use** [16]
History of breast cancer	Abnormal vaginal bleeding between periods
Allergy to this product/ingredient (FD&C yellow No.5 (tartrazine)	Liver tumors or liver disease
Use of other contraceptive pill, vaginal ring, patch, implant, injection, or IUD	History of cancer
Known or suspected pregnancy	
Male patients	

Progestin Only Risk of Thrombosis

- 2016 Systematic Review [17]
  - Evaluated 26 articles including progestin-only pills, injectables, implants, and levonorgestrel IUDs for incidence of VTE, stroke, and acute myocardial infarction
    - 9 cohort studies
    - 17 case-control studies
  - Included studies evaluating the general population as well as those with patients that had increased risk of VTE
    - **Most studies excluded patients with history of thrombosis**
      - **5 studies included women with thrombogenic mutations or history of VTE**

Progestin Only Risk of Thrombosis

- 2016 Systematic Review [17]
  - One study found increased odds of VTE in patients with favor V Leiden (FVL) using depo medroxyprogesterone acetate versus non-users with the mutation
    - OR 2.6, 95% CI 1.8-3.7
  - Odds were similar in women with FVL using levonorgestrel IUDs versus women with FVL that were non-users
    - OR 2.6, 95% (CI 1.2-10.4)
  - Two studies found significantly increased odds of VTE in women using depo medroxyprogesterone in the general population

Progestin Only Risk of Thrombosis

- American College of Obstetricians and Gynecologists (ACOG) Committee Opinion [18]
  - Data suggests progestin-only contraception is generally safe with no or minimal VTE risk
  - References previously mentioned systematic review showing no statistically significant increase compared with non users
  - ACOG supports OTC access to hormonal contraception

Patient Case

AG is a 28 year old female with a history of VTE but not currently on anticoagulation. She complains of heavy menstrual bleeding and would like to pursue contraceptive options for this. Which of the following is the best option for AG?

A. Injectable medroxyprogesterone
B. Copper IUD
C. Progestin-only pill
D. Estrogen patch

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B. Copper IUD
C. Progestin-only pill
D. Estrogen patch

Summary

- Estrogen containing and injectable progesterone contraceptives have a documented increase risk of thrombosis
- Many non-hormonal options are available for patients with a risk or history of thrombosis
- Patients may continue hormonal contraception while on anticoagulation
- Progestin only contraception (excluding injection) does not appear to show increase risk of VTE. Randomized control trials may be needed to further confirm this.
- Over the counter progestin only contraception may be a safe option for patients with a risk or history of VTE

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Need More Information?

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