

EDUCATION

64-68	University of Chicago	Biochemistry
68-72	University of Pittsburgh	MD
72-75	Harvard (Deaconess/Brigham)	Internal Medicine
75-78	UCONN	Hematology

EMPLOYMENT

- 78-90 30% UCONN FACULTY - CLINICAL/TEACHING
70% VA - RESEARCH (COAG/IMMUNOLOGY/CANCER
- 90-01 50% UCONN - TEACHING & MARROW TRANSPLANT
50% RED CROSS - ASSOC MED DIRECTOR/DIRECTOR
OF HLA LAB/MED DIRECTOR NEW ENGLAND
REGION NATL MARROW DONOR PROGRAM
- 01-18 20% UCONN TEACHING
80% ST FRANCIS/YALE CANCER CENTER - HEMA-
TOLOGY & DIRECTOR COAGULATION PGM

OVERVIEW OF BLOOD CLOTTING AND ANTICOAGULATION

WHAT IS WORSE, CLOTTING OR BLEEDING?

BOTH CAN BE SERIOUS BUT “BLEEDING ALWAYS STOPS”

UNLESS BLEEDING IS IN A CONFINED SPACE (e.g. SKULL) OR IS MASSIVE, MOST PEOPLE SURVIVE BLEEDING

CLOTS, HOWEVER OFTEN LEAD TO SERIOUS OR LIFE-THREATENING ORGAN DAMAGE (MYOCARDIAL INFARCTION, STROKE, PULMONARY EMBOLISM etc.

SO, IN GENERAL, CLOTTING IS MORE DANGEROUS THAN BLEEDING

COMPONENTS OF BLOOD

RED BLOOD CELLS (CARRY OXYGEN) 5,000,000/ μ l

WHITE BLOOD CELLS (FIGHT INFECTION) 3000/ μ l

PLATELETS (PREVENT BLEEDING) 200,000/ μ l

PLASMA (CONTAINS ALL CLOTTING FACTORS, as well as
PROTEINS, FATS, SUGARS, HORMONES, etc.

WHAT PREVENTS THE BLOOD FROM CLOTTING?

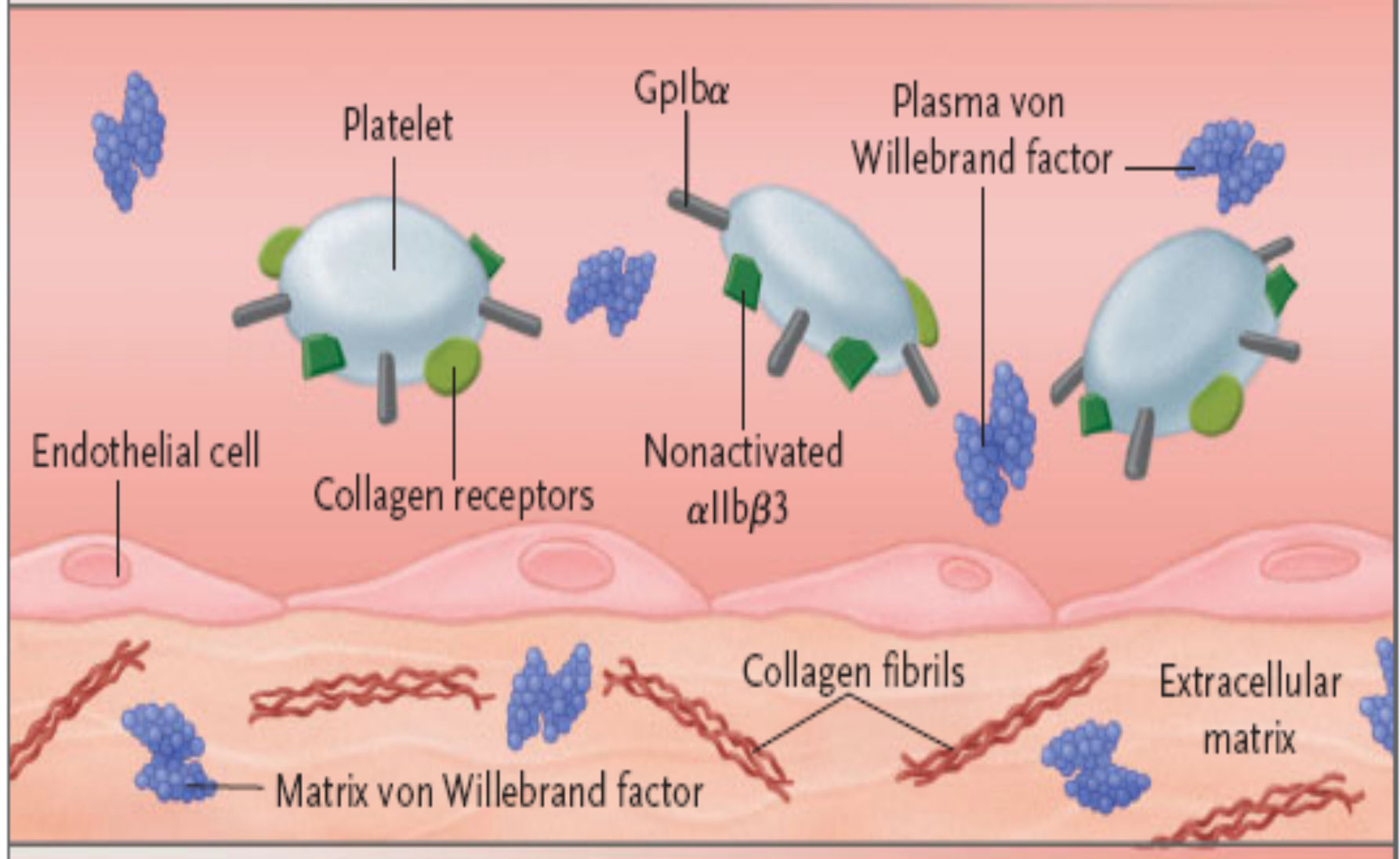
FLOWING BLOOD PREVENTS PLATELETS FROM
ADHERING TO BLOOD VESSEL WALL

INTACT ENDOTHELIAL SURFACE PREVENTS
PLATELETS FROM CONTACTING COLLAGEN

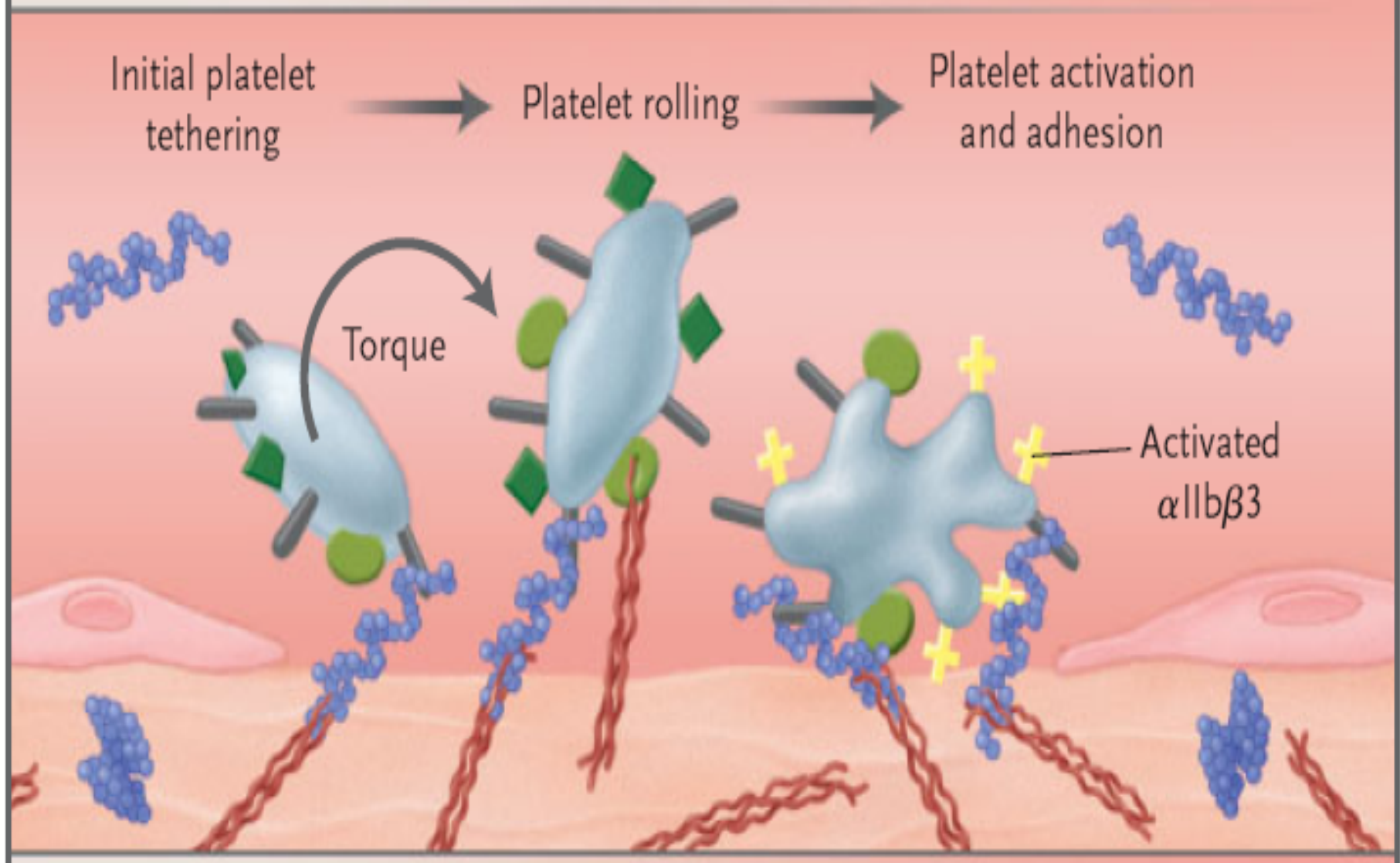
ENDOTHELIAL CELLS SECRETE THE PLATELET
INHIBITOR PGI₂

NATURAL ANTICOAGULANTS IN THE BLOOD
HEPARIN, ANTITHROMBIN

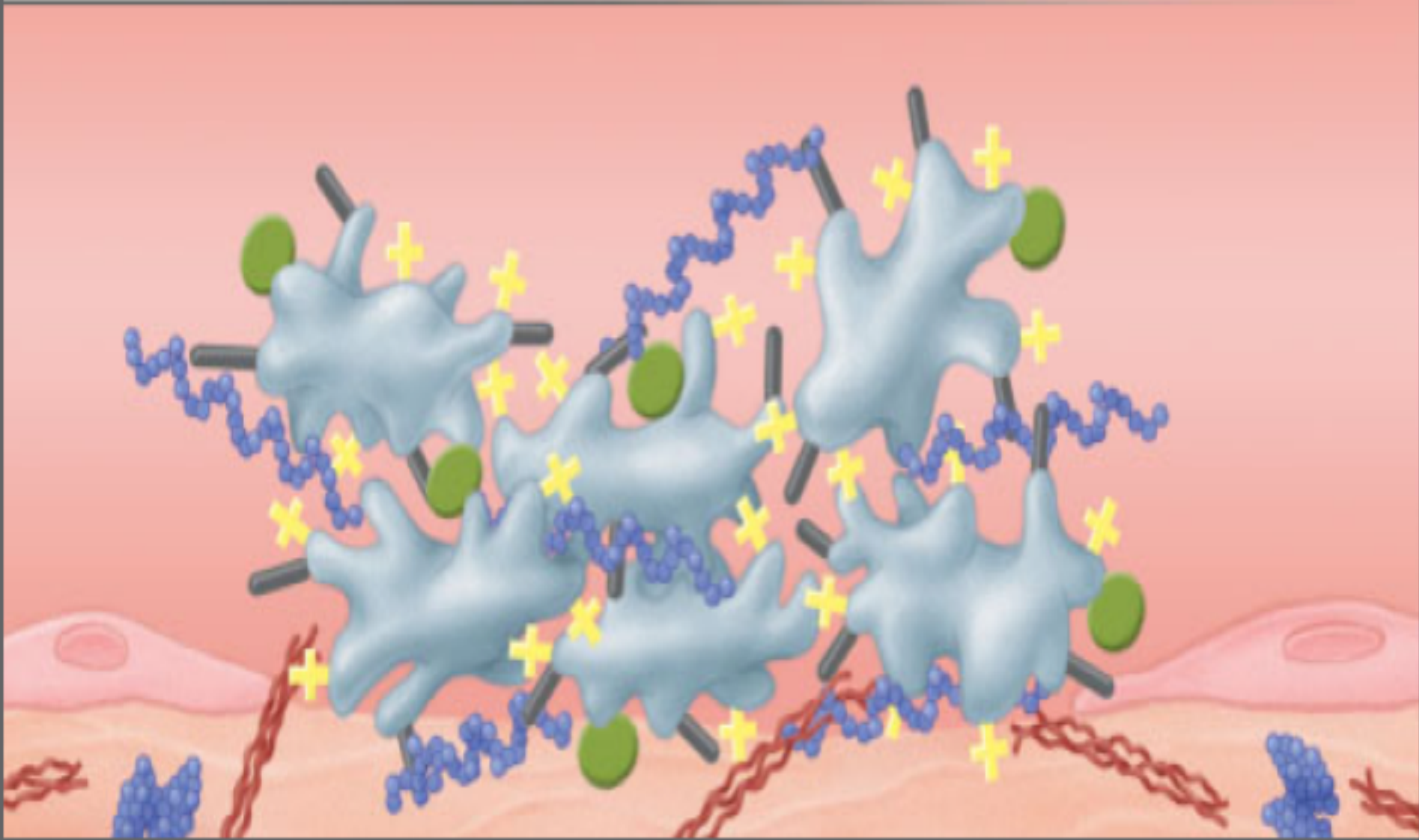
A Intact vessel wall

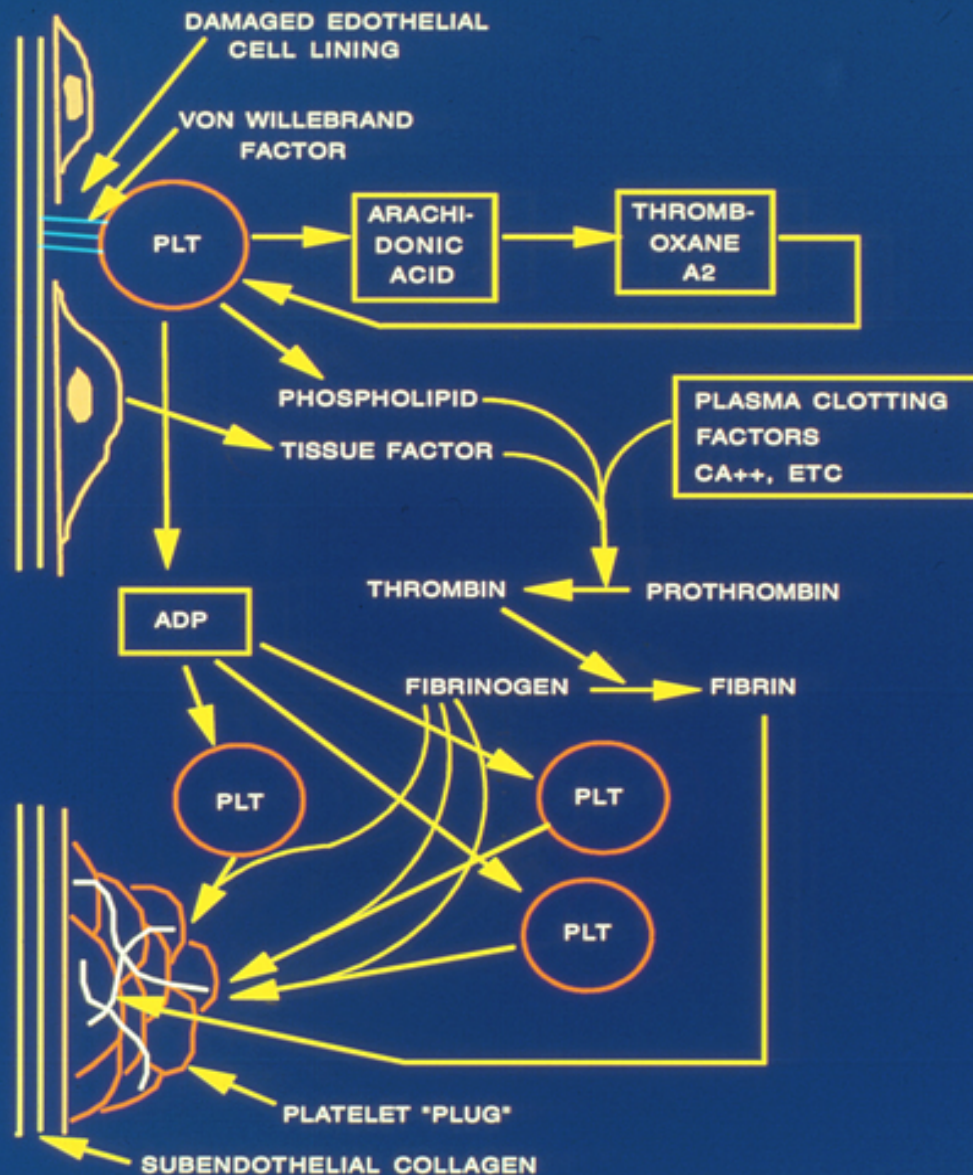


B Damaged vessel wall



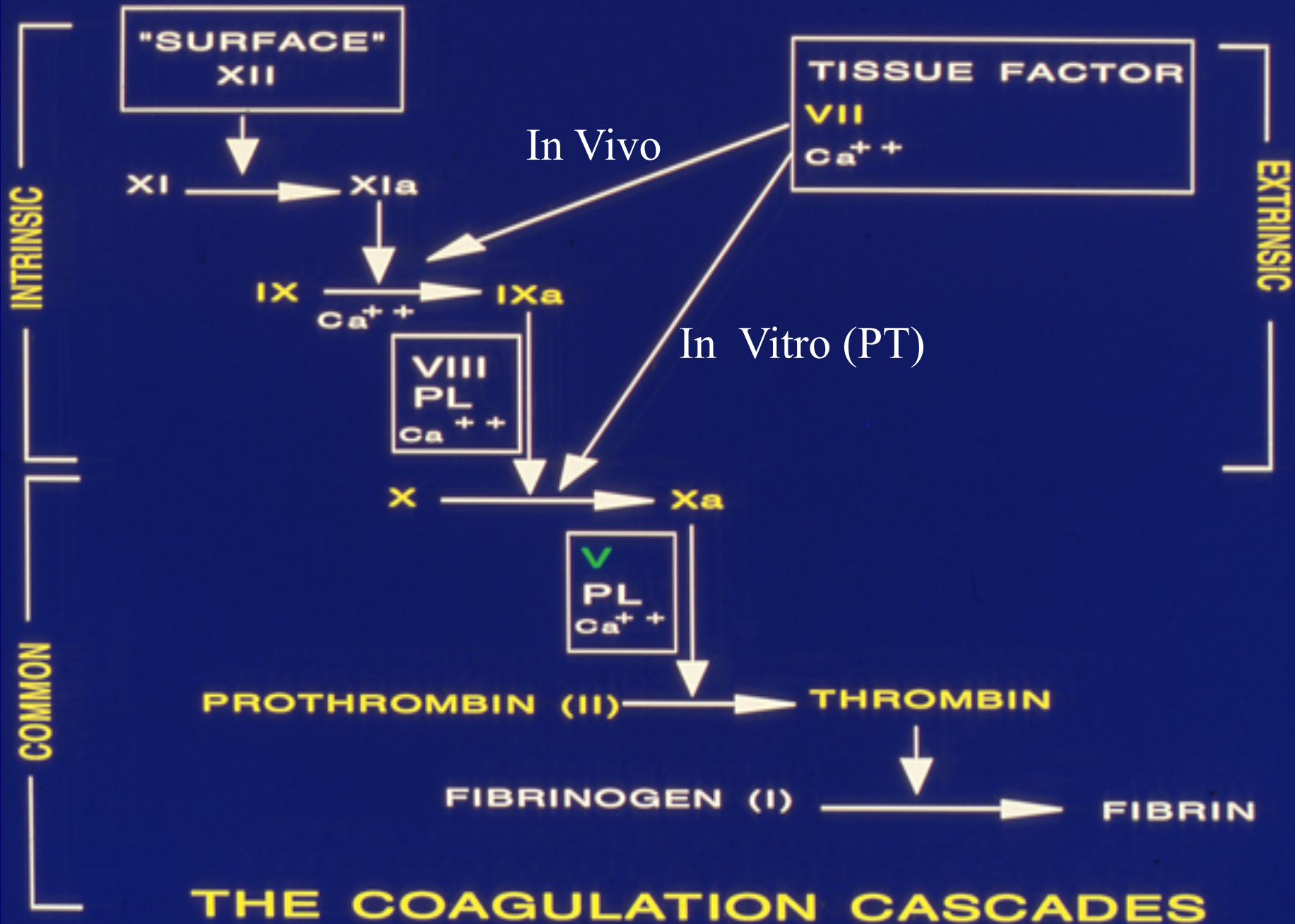
C Platelet-plug formation





OVERVIEW OF HEMOSTASIS

(MODIFIED FROM ZUCKER, ET AL. SCI AM 242:86, 1980)



PLATELET-RELATED BLEEDING

DECREASED PLATELET NUMBERS

ITP

BONE MARROW FAILURE

ABNORMAL PLATELET FUNCTION

CONGENITAL PLATELET ABNORMALITIES

VON WILLEBRAND DISEASE

DRUGS (eg ASPIRIN)

USUALLY CAUSES BRUISING OR PETECHIAE (RED SPOTS ON SKIN)

IF SEVERE, MAY REQUIRE PLATELET TRANSFUSION

Petechiae



Purpura



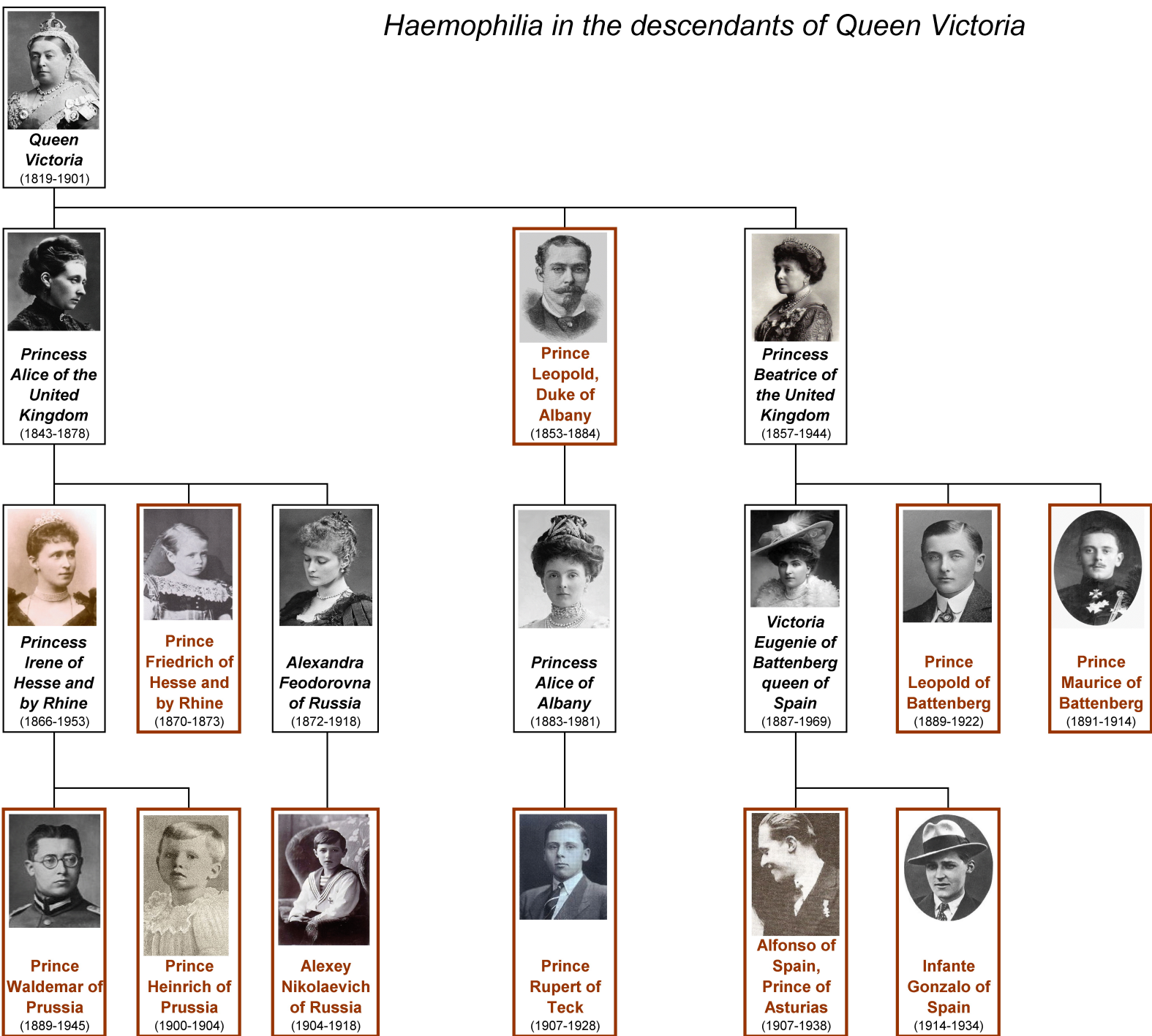
BLEEDING DUE TO FACTOR DEFICIENCIES

OFTEN MORE SEVERE AND CAN LEAD TO SPONTANEOUS
BLEEDING INTO JOINTS

MAY REQUIRE INFUSIONS OF PLASMA OR FACTOR
CONCENTRATES



Haemophilia in the descendants of Queen Victoria



Risk Factors for Arterial Thrombosis (Stroke, Heart Attack)

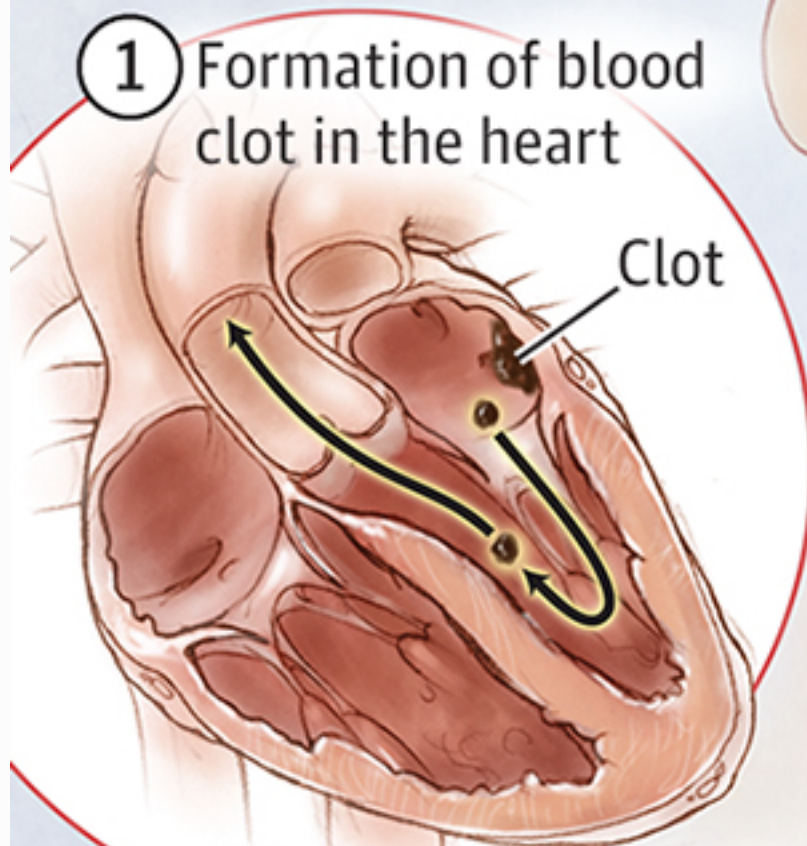
Atrial Fibrillation

Mechanical Heart Valves

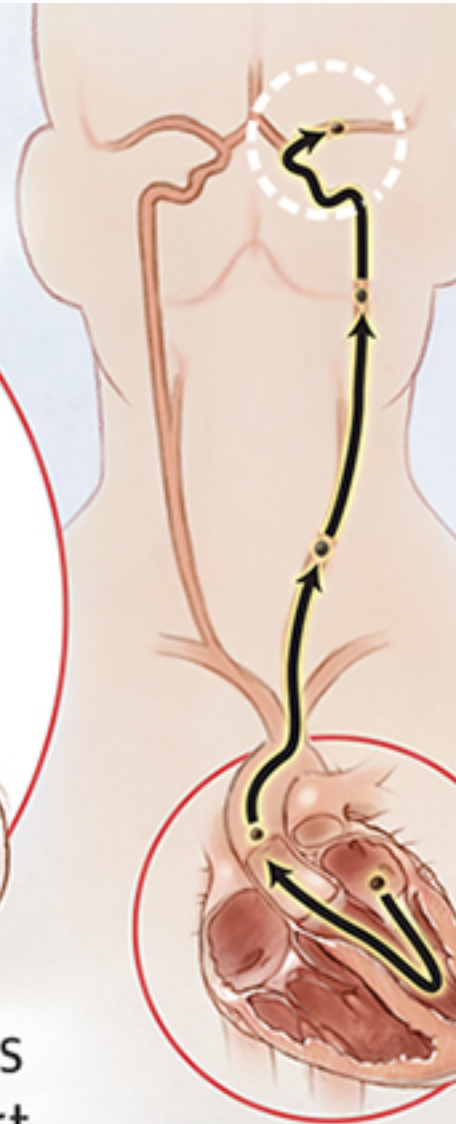
Atherosclerosis

Atrial Fibrillation

- 1 Formation of blood clot in the heart



- 2 Blood clot travels through the heart

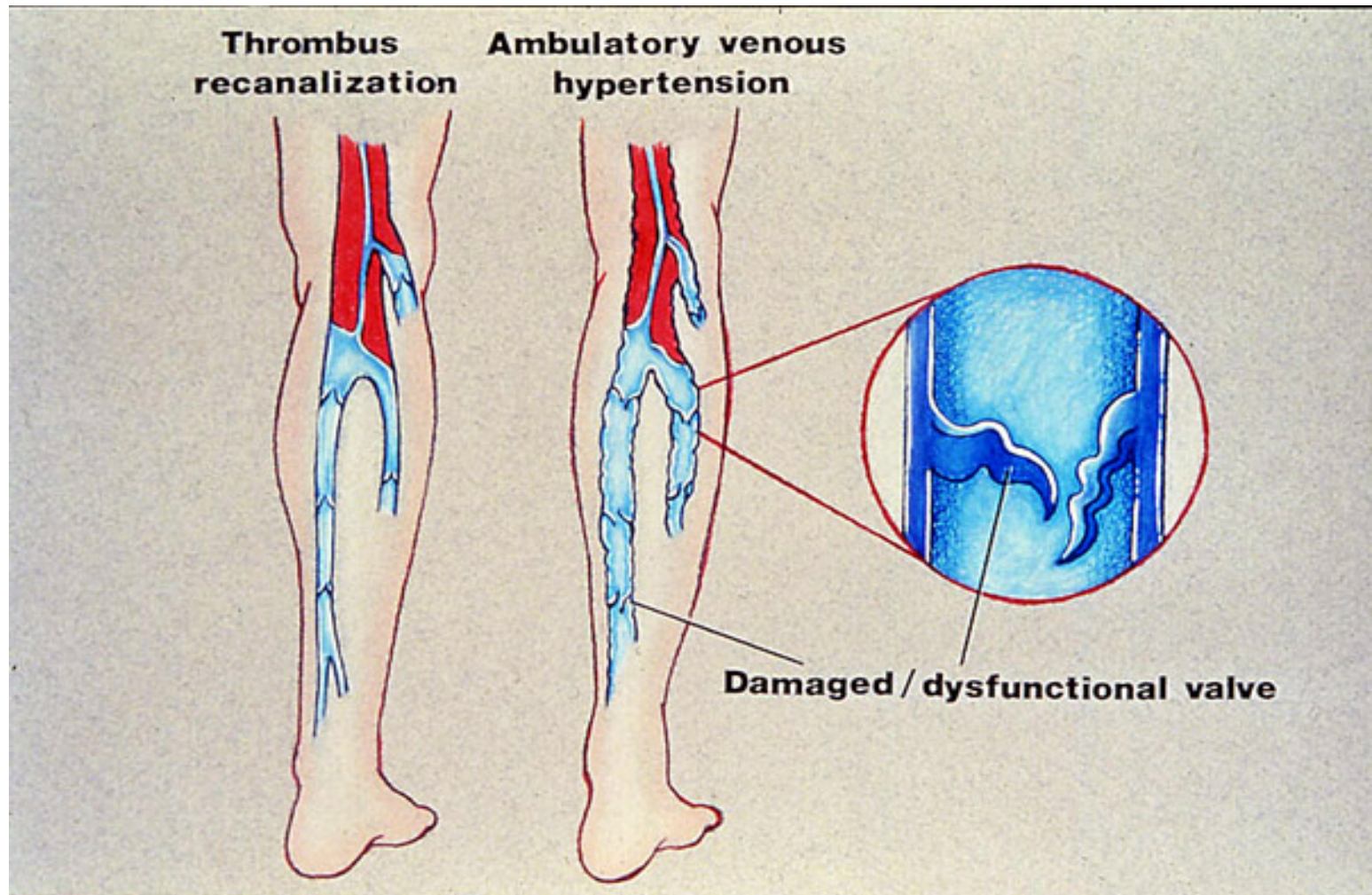


Major Risk Factors for Venous Thrombosis

- Acquired
 - Bed rest
 - Plaster cast
 - Trauma
 - Major Surgery
 - Orthopedic Surgery
 - Malignancy
 - OCP/HRT/pregnancy
 - Myeloproliferative
 - Phospholipid dependent antibodies
 - Increase Factor VIII, TAFI, IX, XI
 - Immobilization (airplane travel)
- Inherited
 - Factor V Leiden (common)
 - Prothrombin G20210A
 - PC, PS, AT deficiency
 - Dysfibrinogenemia
 - Factor XIII 34 val
 - Increase Factor VIII, TAFI, IX, XI



Mechanism of Post-phlebitic Syndrome



Severe Post-phlebitic Syndrome



COMMON DRUGS USED TO PREVENT BLOOD CLOTTING

ASPIRIN

WARFARIN (COUMADIN)

DIRECT ORAL ANTICOAGULANTS (XARELTO, PRADAXA, etc)

HEPARIN

LOW MOLECULAR WEIGHT HEPARIN (LOVENOX, etc)

HEPARIN

INACTIVATES MULTIPLE CLOTTING FACTORS

ACTS IMMEDIATELY

EFFECTIVE FOR BOTH VENOUS AND ARTERIAL CLOTS

AVAILABLE IN 2 FORMS:

UNFRACTIONATED HEPARIN DERIVED FROM PIG TISSUE
GIVEN BY IV INFUSION IN HOSPITAL OR CLINIC
MUST BE MONITORED WITH FREQUENT BLOOD TESTS

SYNTHETIC (LOW MOLECULAR WEIGHT) HEPARIN
GIVEN SUBCUTANEOUSLY IN FIXED DOSE BASED ON WT
MAY BE USED TO PREVENT CLOTTING OR TO TREAT
ACTIVE CLOTTING

Aspirin

Aspirin inhibits platelet activation and the formation of the platelet plug

Aspirin's effect on platelets is permanent so all platelets are inhibited for their lifetime (10 days)

Large doses of aspirin also block the production of the PGI₂ anti platelet factor by the vessel wall and cancel out the antiplatelet activity produced by small aspirin doses

Therefore, small doses (81 mg) are more effective at preventing clots than larger doses (325 mg)

Aspirin is more effective preventing arterial thrombosis (stroke, heart attack) than venous thrombosis

Warfarin

Discovered when it was noticed that cows had blood in milk

Spoiled grain had substance that prevented blood from clotting
(Warfarin named after Wisconsin Animal Research facility)

Blocks vitamin K and decreases production of vitamin K-dependent clotting factors

Patients taking Warfarin must eat a diet with consistent amounts of vitamin K (mostly green vegetables) and must be tested frequently to be sure they are getting the correct dose of Warfarin

When well-managed, Warfarin is very effective at preventing arterial and venous clots

DOACs

Xarelto, Pradaxa, Eliquis, etc

True anticoagulants (directly inhibit clotting factors)

Not dependent on vitamin k inhibition so no diet restrictions

Given in standard dose (no testing available, no dose adjustments) - not sure if effective in patients >250 lbs

Not effective in patients with severe clotting risks (artificial heart valves, hyper coagulable conditions)

Expensive. ? insurance coverage

No antidote if bleeding occurs