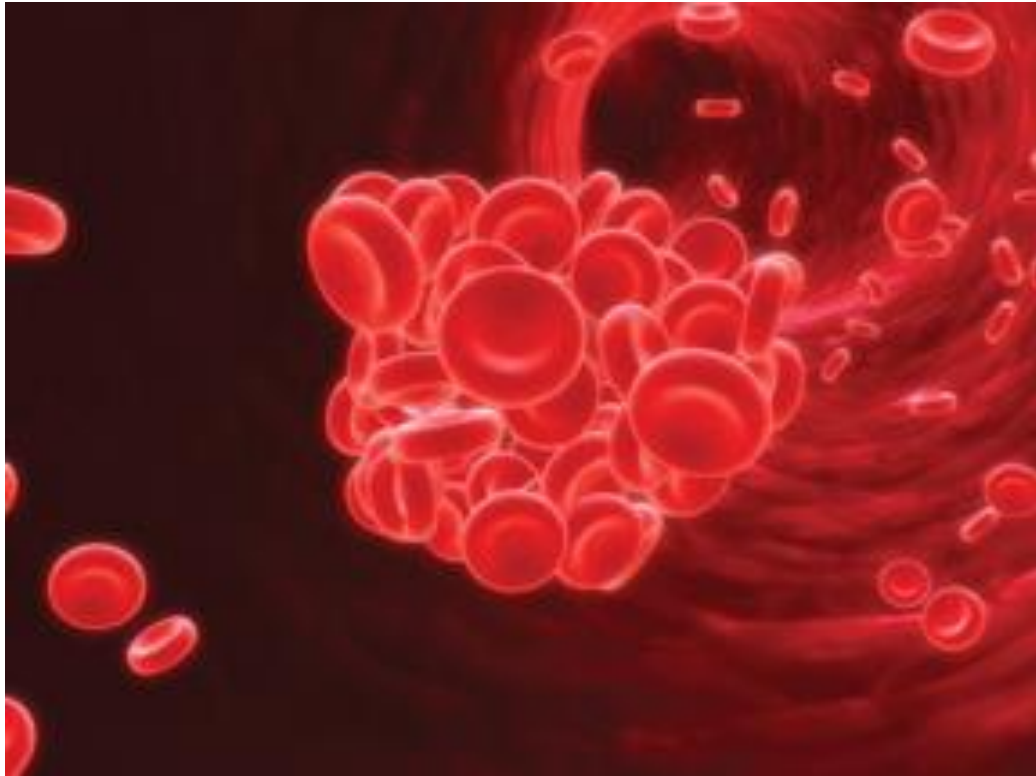


# Anticoagulation – From Warfarin to Newer Agents



Brian J Barkow, PharmD, CSP, CDE  
Ambulatory Care Pharmacist  
Doctor of Pharmacy (PharmD)  
Certified Specialty Pharmacist (CSP)  
Certified Diabetic Educator (CDE)

# Lecture Outline

- Speaker Background (5 minutes)
- Anticoagulation: What Is It and Why Do It? (50-60 minutes)
- Break (10 minutes)
- Agents for Anticoagulation: Old and New (30-40 minutes)
- Wrap-up and follow up questions (5-10 minutes)

# Speaker Background

- Green Bay native
- 3rd career pharmacist (others: pastoral ministries & public education)
- Went into pharmacy because of familial seeming medication misuse
- Graduated University of Arizona with a Doctor of Pharmacy degree
- Additional community residency done through UW Madison – at Streu's Pharmacy in Green Bay – Transition of Care service developed with Bellin Health
- Two and a half years in Specialty Pharmacy – Certified Specialty Pharmacist
- Ambulatory Care Pharmacist with Bellin Health – Goal of reducing costs through preventative and intervening medication care
- Team Facilitator of Ambulatory Care Pharmacy including Anticoagulation Clinic

# Summary – Main Points

- Blood is life – Coagulation and Anticoagulation are means to help address the system not functioning as it should
- Clots form in different parts of the vascular system and for different reasons, therefore the medications used to address them are different, although there is overlap
- Warfarin has been a gold standard of an anticoagulant, however; there are other agents, and DOACs are getting nod over warfarin in some conditions (atrial fibrillation)
- Although there are many different choices, continue to question if what you are on is best for you

Anticoagulation:

What Is It?

And Why Do It?

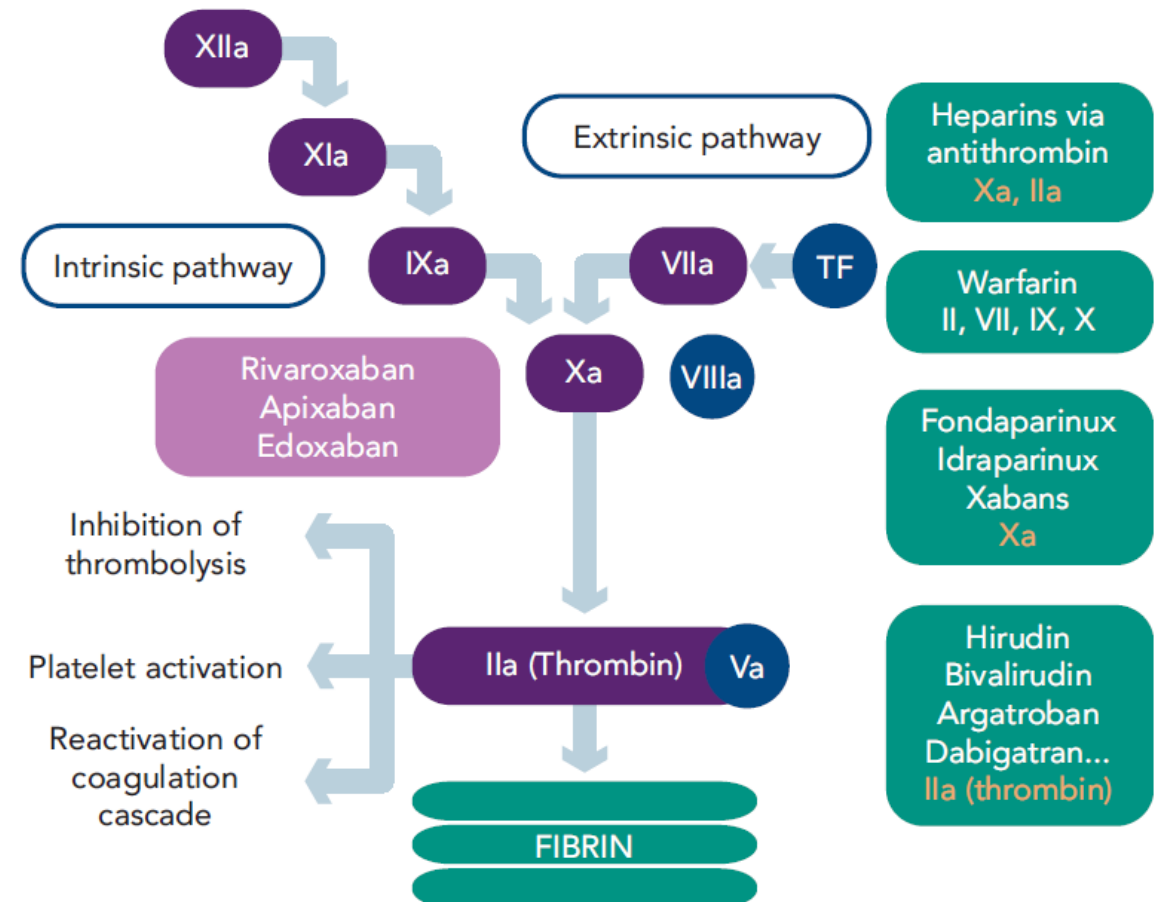
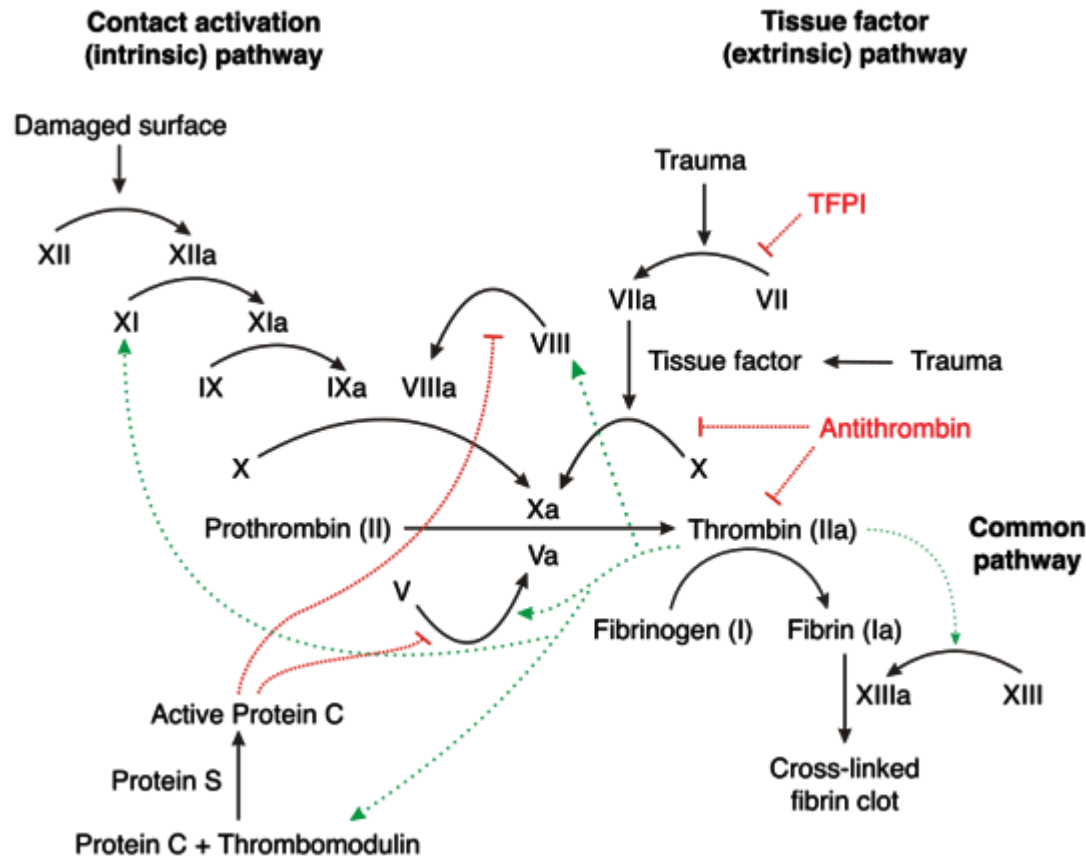
# Blood = Life

- Leviticus 17:14a “Because the life of every creature is its blood.”
- Blood serves a number of functions in the body, but basically it needs to:
  - Flow – to move nutrients out to the body and bring waste products for elimination
  - Clot – to repair the internal tubular system so it can continue to flow
    - This process is known as “Coagulation”
- “Anticoagulation” is slowing down or preventing the process as for some reason it is happening not the way the system was intended



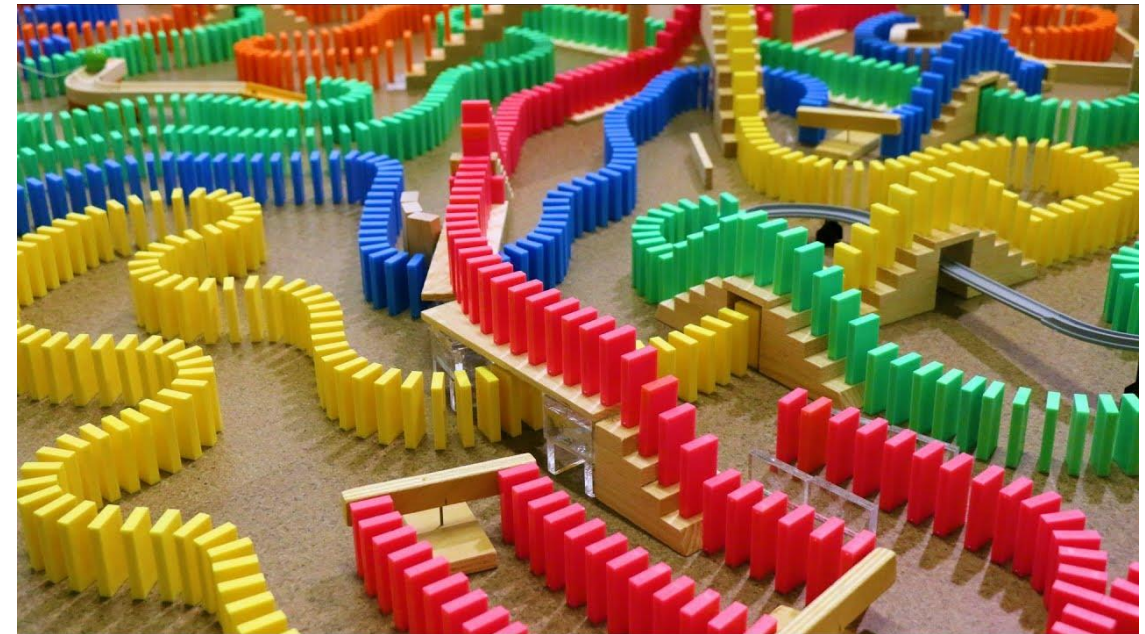
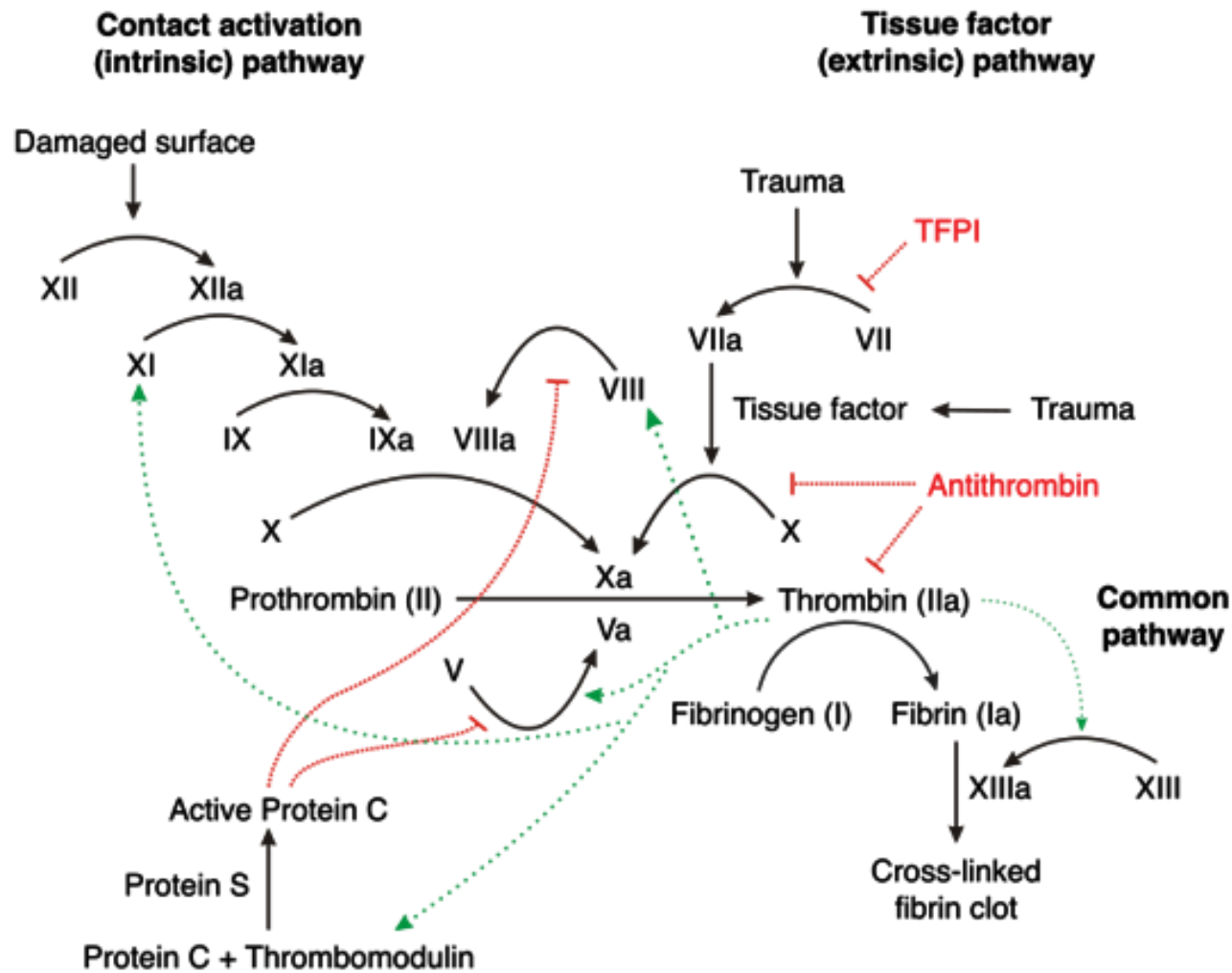
# Anticoagulation – Prevention of Clots

Figure 1: Action of Anticoagulants in the Coagulation Cascade



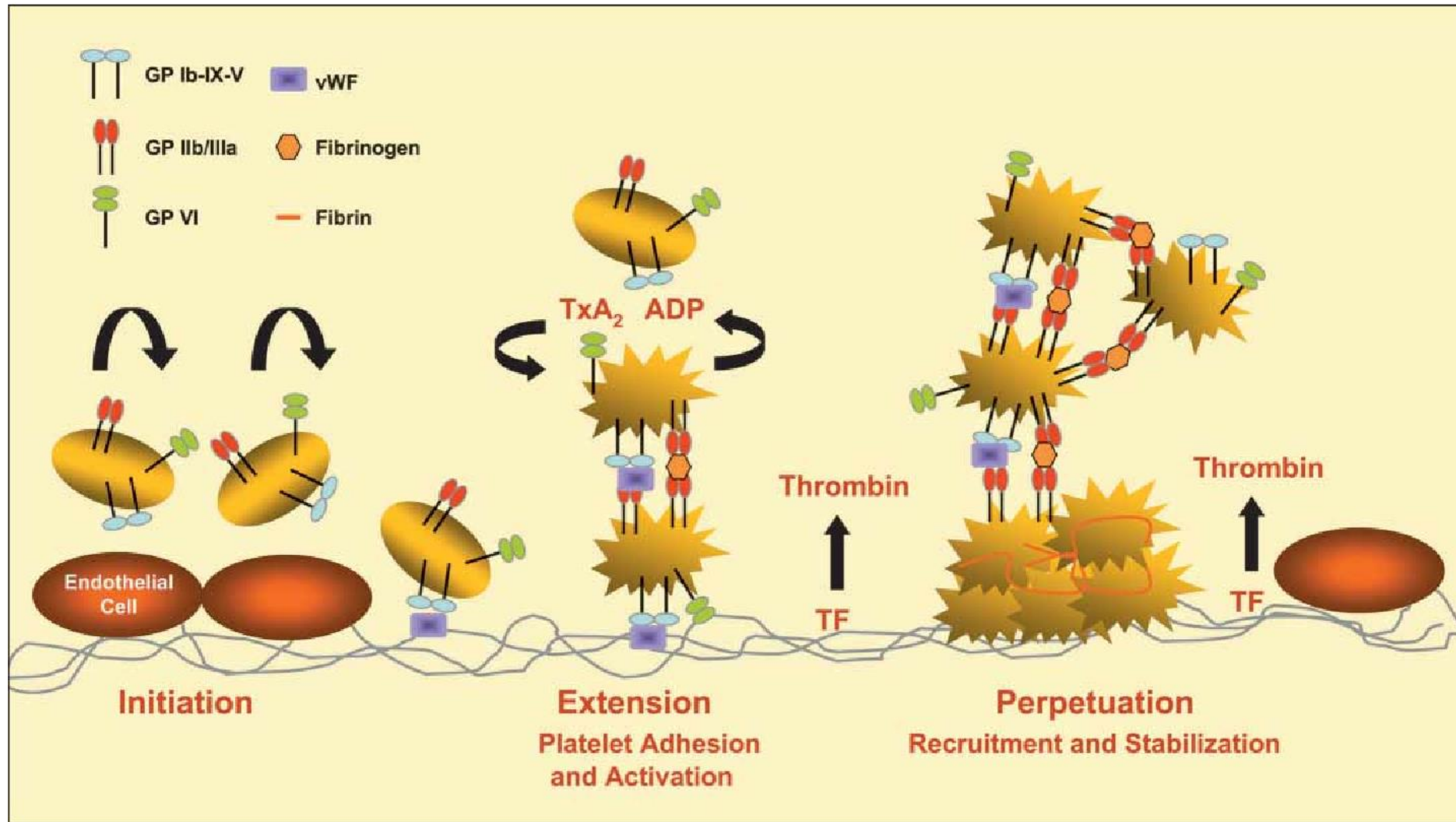
Note that edoxaban is not registered for use in the EU and the USA at the time of publication.

# Anticoagulation – Coagulation Cascade



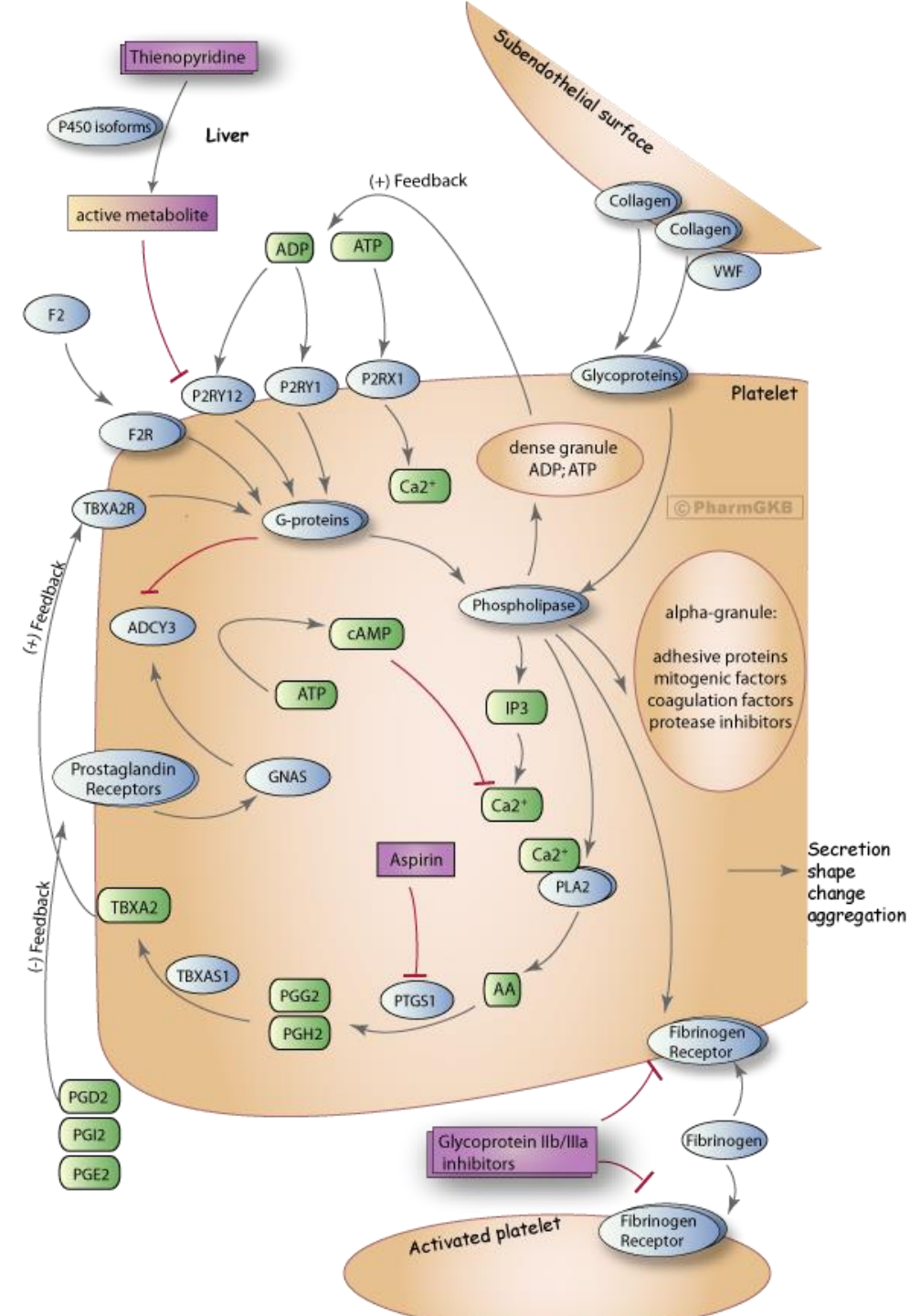


# Anticoagulation – Platelet Activation & Aggregation



# Anticoagulation – Platelet Activation & Aggravation

Inside and on the platelet –  
where Aspirin, Clopidogrel,  
Ticagrelor, Prasugrel, and others  
work



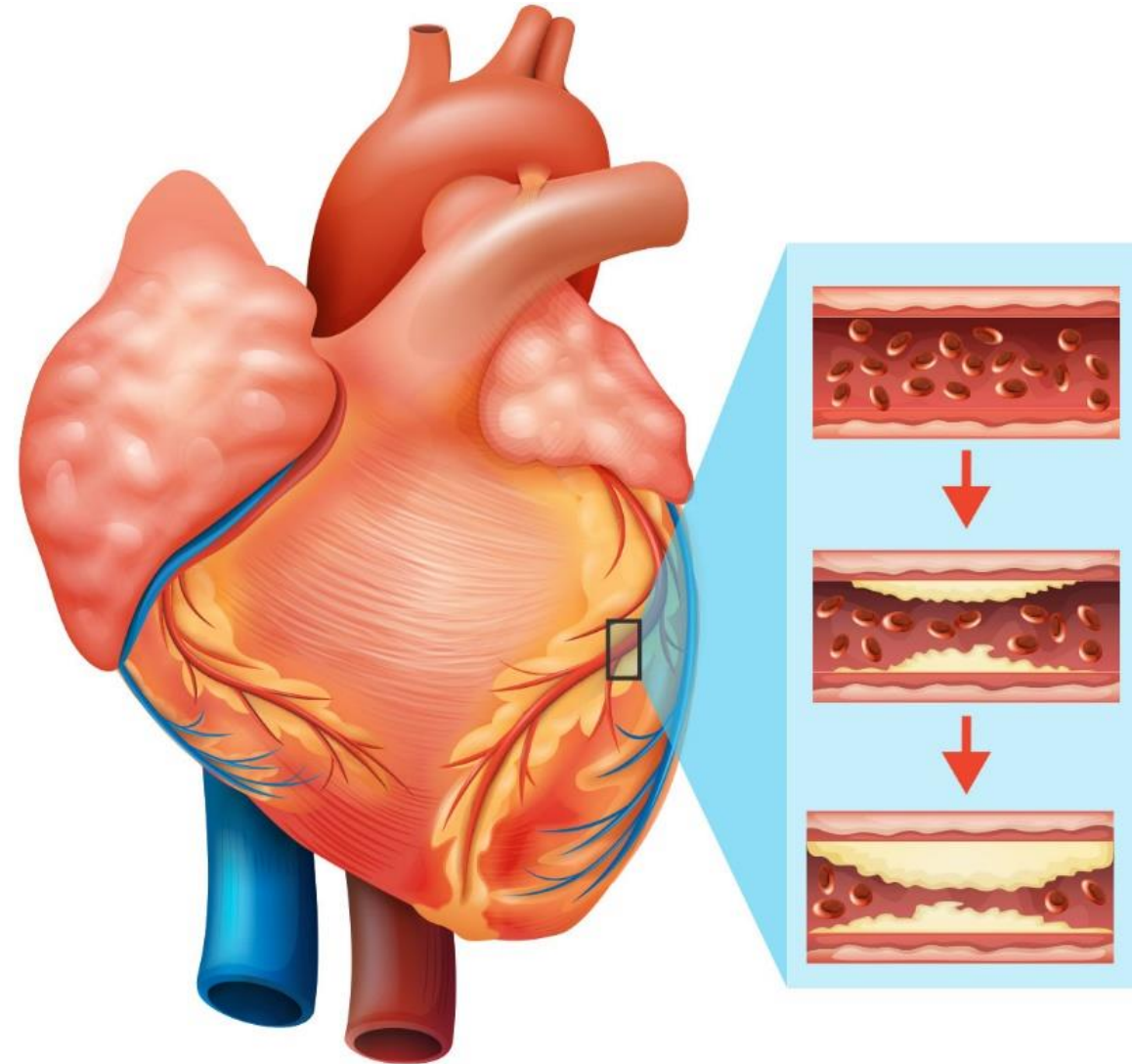
# Certain Conditions Increase Body's Risk of Forming Clots Where We Don't Want Them

- Heart Attack, Vascular Disease or Stroke (non-cardioembolic)
- Heart Valve Replacement (Stroke – cardioembolic)
- Atrial Fibrillation (Stroke – cardioembolic)
- Venous Thromboembolisms (VTEs - Clots in venous system)
  - Deep Vein Thrombosis (DVT)
  - Pulmonary Embolism (PE)
  - VTEs Any Locations
    - Factor V Leiden
    - Antiphospholipid syndrome
    - Others: Protein S or C deficiency, Elevated Factor VIII levels, Factor II mutation

Heart Attack,  
Vascular Disease,  
&  
Non-Cardioembolic Stroke

# Heart Attack – Myocardial Infarct (MI)

- Some number of arteries, which feed the heart, become blocked off with plaque build up
- Results in down-stream heart tissue being starved for oxygen
- Heart then “screams out” that it “suffocating”





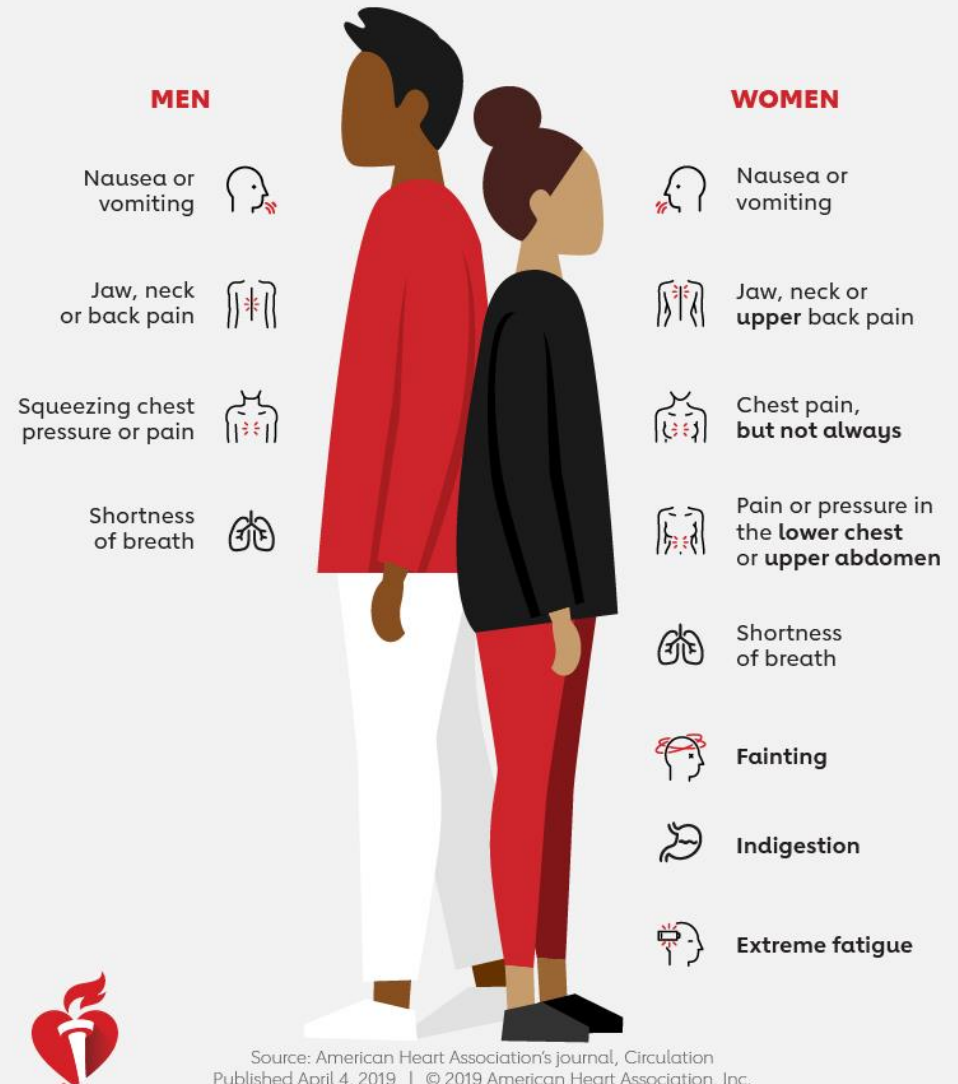
# Heart Attack – Signs & Symptoms

- Different between males and females
- Generally common signs:
  - Chest discomfort
  - Left arm tingling or numb
  - Shortness of breath
- Things to consider:
  - Sometimes feels like heart burn
- If Heart Attack suspected:
  - Most important – get to ED
  - If able – get aspirin ~ 325 mg in

## HEART ATTACK SYMPTOMS: MEN VS. WOMEN

By American Heart Association News

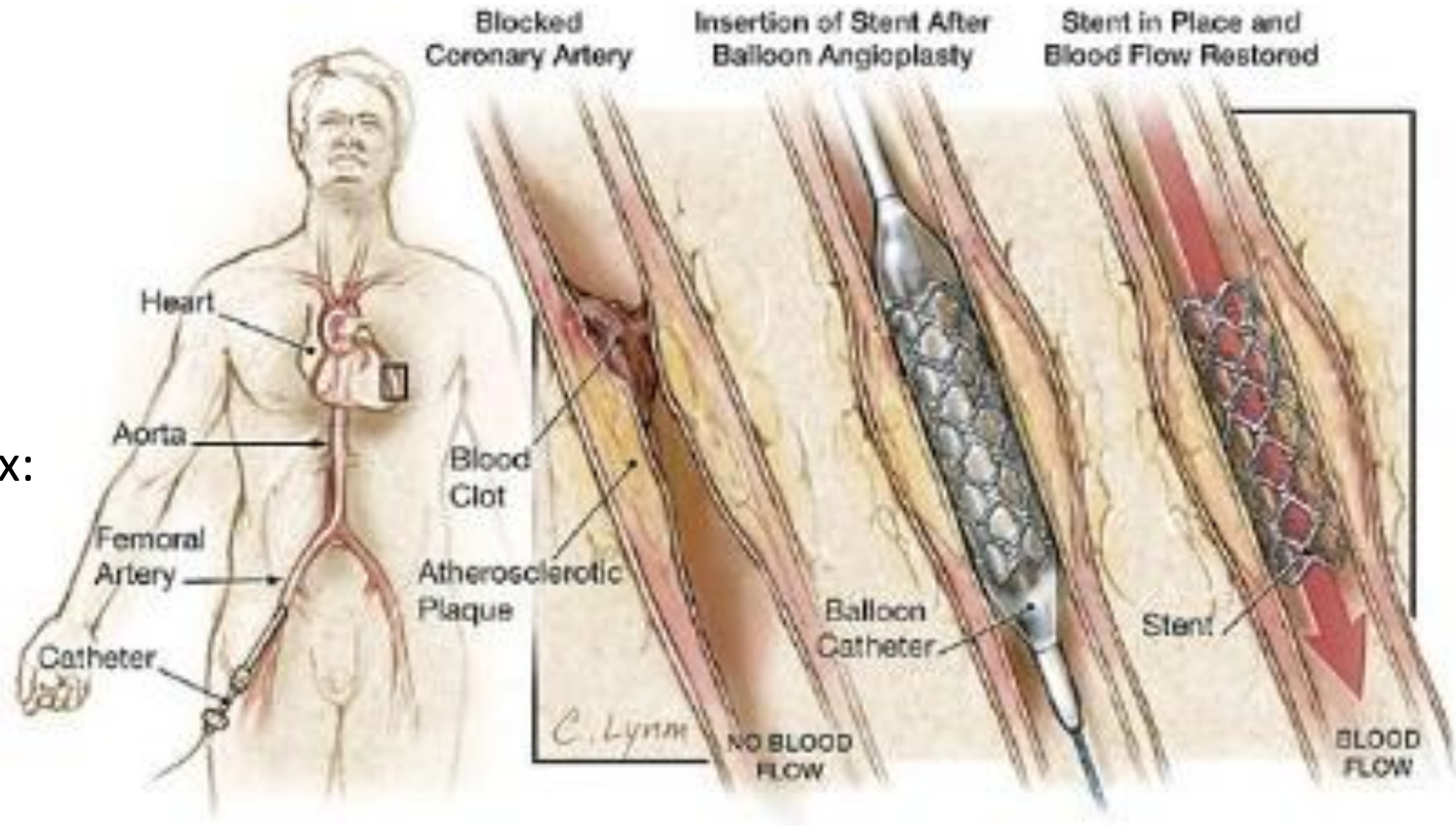
The most common symptom of a heart attack for both men and women is chest pain. But women may experience less obvious warning signs.



# Heart Attack – Percutaneous Coronary Intervention (PCI) aka – Stent

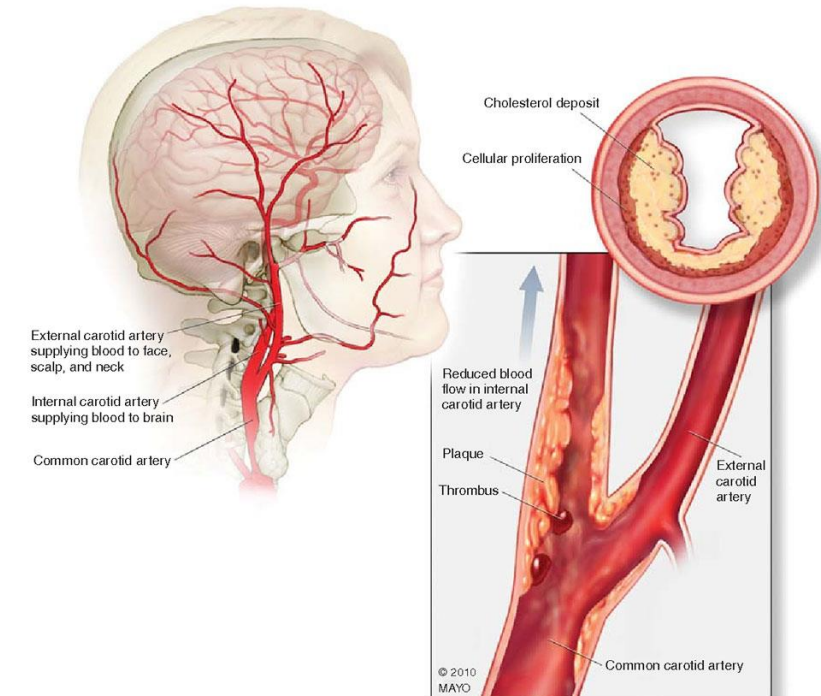
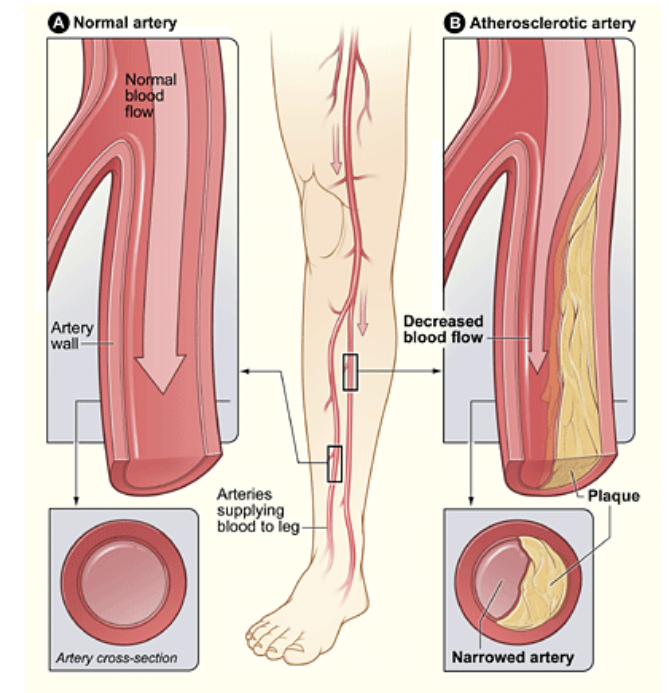
Medications post MI with stent:

- Aspirin 81 mg daily
- Clopidogrel 75 mg daily (or other P2Y12 antiplatelet) x 6-12 months
- High intensity statin – Ex: Atorvastatin 40-80 mg daily
- Beta-blocker
- ACE-I or ARB



# Vascular Disease

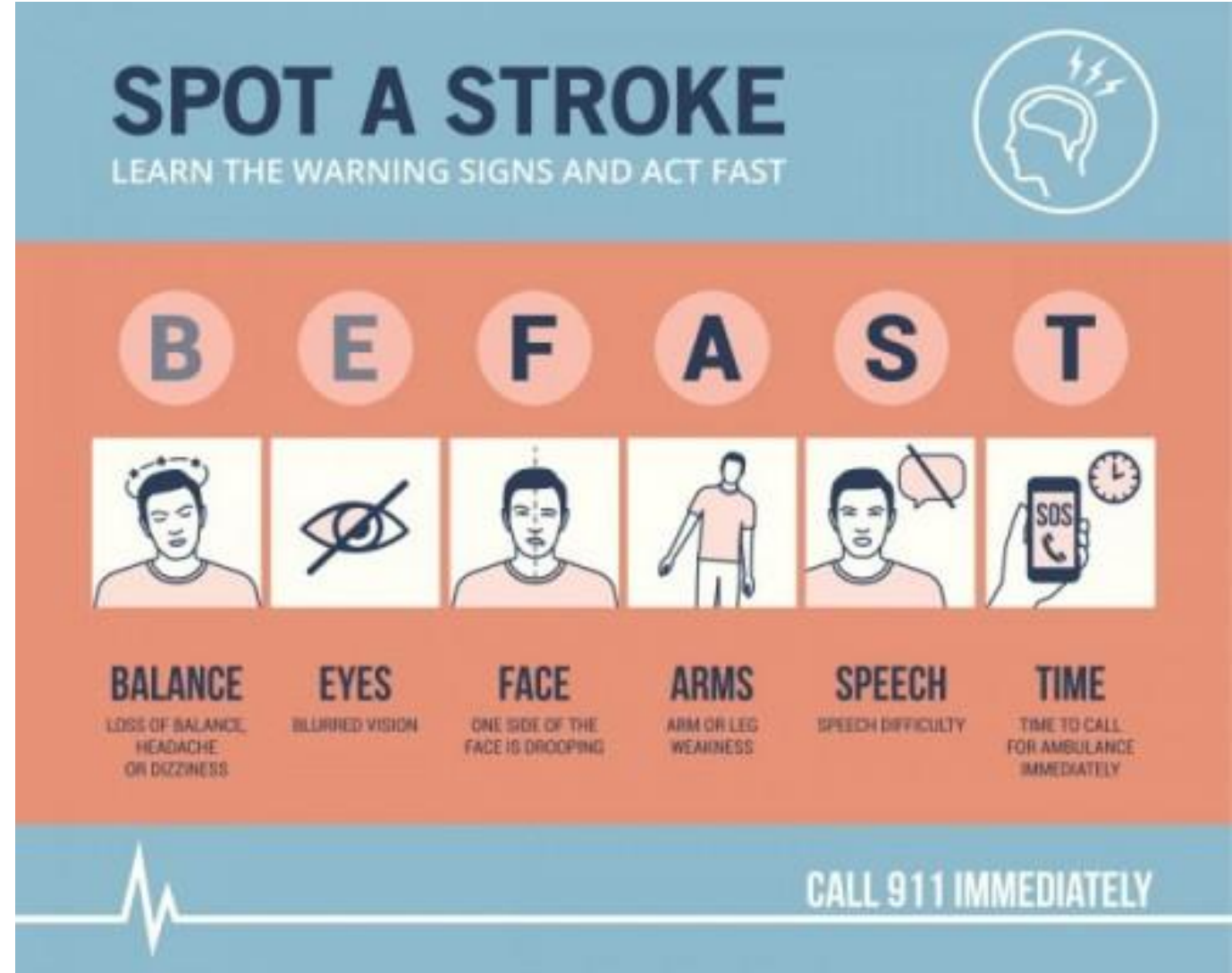
- Includes:
  - Coronary Artery Disease (CAD)
    - CAD can lead to MI
  - Plaque build up in any vascular structure:
    - Carotid artery
    - Peripheral Artery Disease (PAD)
- Treatment may include:
  - Stent placement
  - Endarterectomy – surgical removal of plaque
  - High intensity statin (ex: atorvastatin 40-80 mg)
  - Antiplatelet use (typical: Aspirin 81 mg)
  - New studies showing promise with rivaroxaban (Xarelto) 2.5 mg twice daily with Aspirin 81 mg daily
  - May include some lower line therapy medications:
    - Pentoxifylline – May improve blood flow
    - Cilostazol – Maybe helps in pain while walking





# Stroke

- Signs of stroke:
  - Drooping of face
  - Slurring of speech
  - One side body action decrease
- Call 911 ASAP!
- If time symptoms started is known, mark it
- Give aspirin in stroke?
  - NO!
- Ischemic (clot) vs. Hemorrhagic (bleeding)



# Cardioembolic Vs. Non-Cardioembolic Stroke

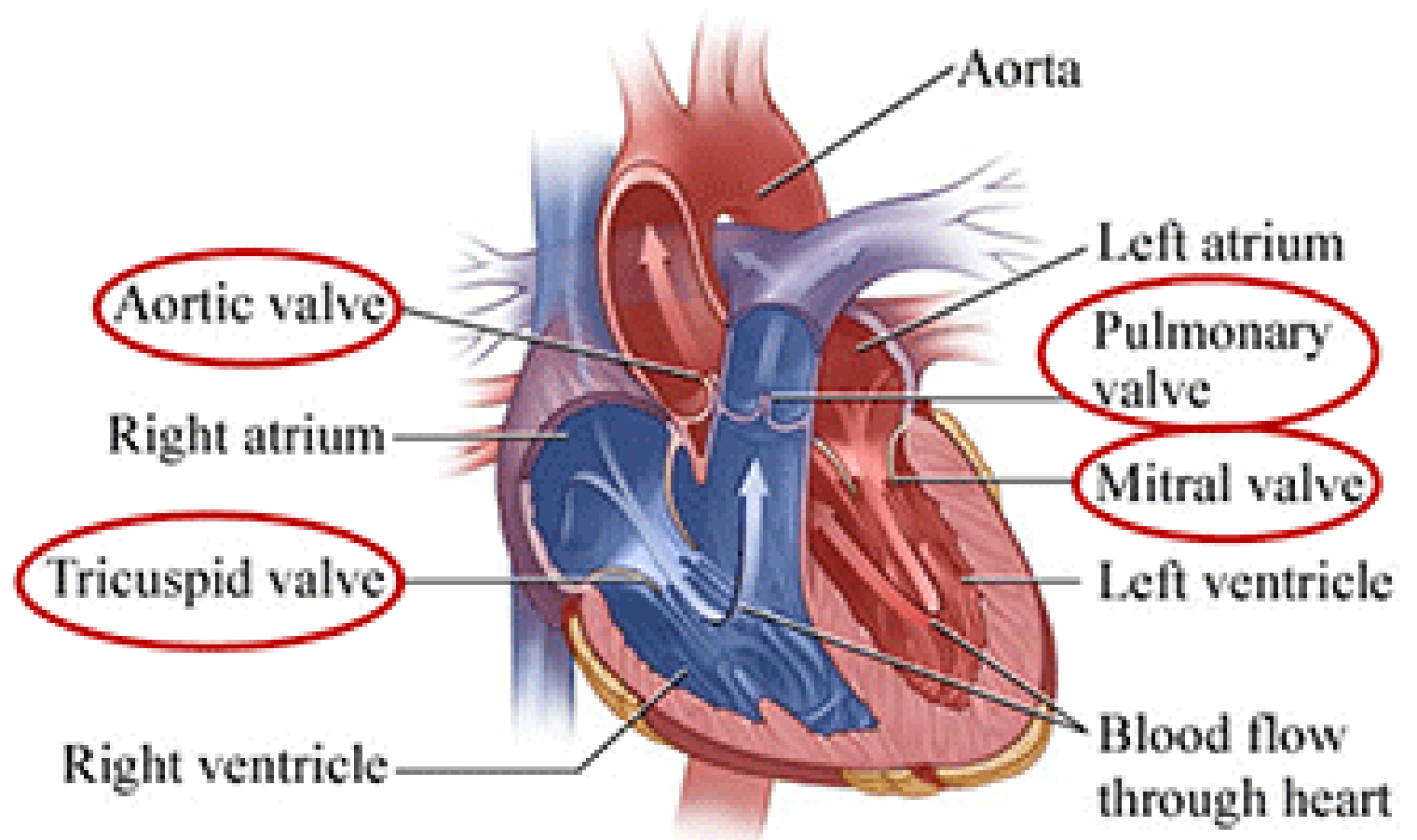
- Cardioembolic – “Clot originating from heart”
- Non-Cardioembolic – “Clot not originating from heart”
- Stroke can be caused by either, however; depending upon if source is known, treatment is different
- Non-Cardioembolic – antiplateletes, specifically aspirin, are by far preferred agents – other oral anticoagulants only increase risk of bleeding
- Cardioembolic – oral anticoagulants, generally warfarin, is agent of choice

# Heart Valves

# Heart Valves

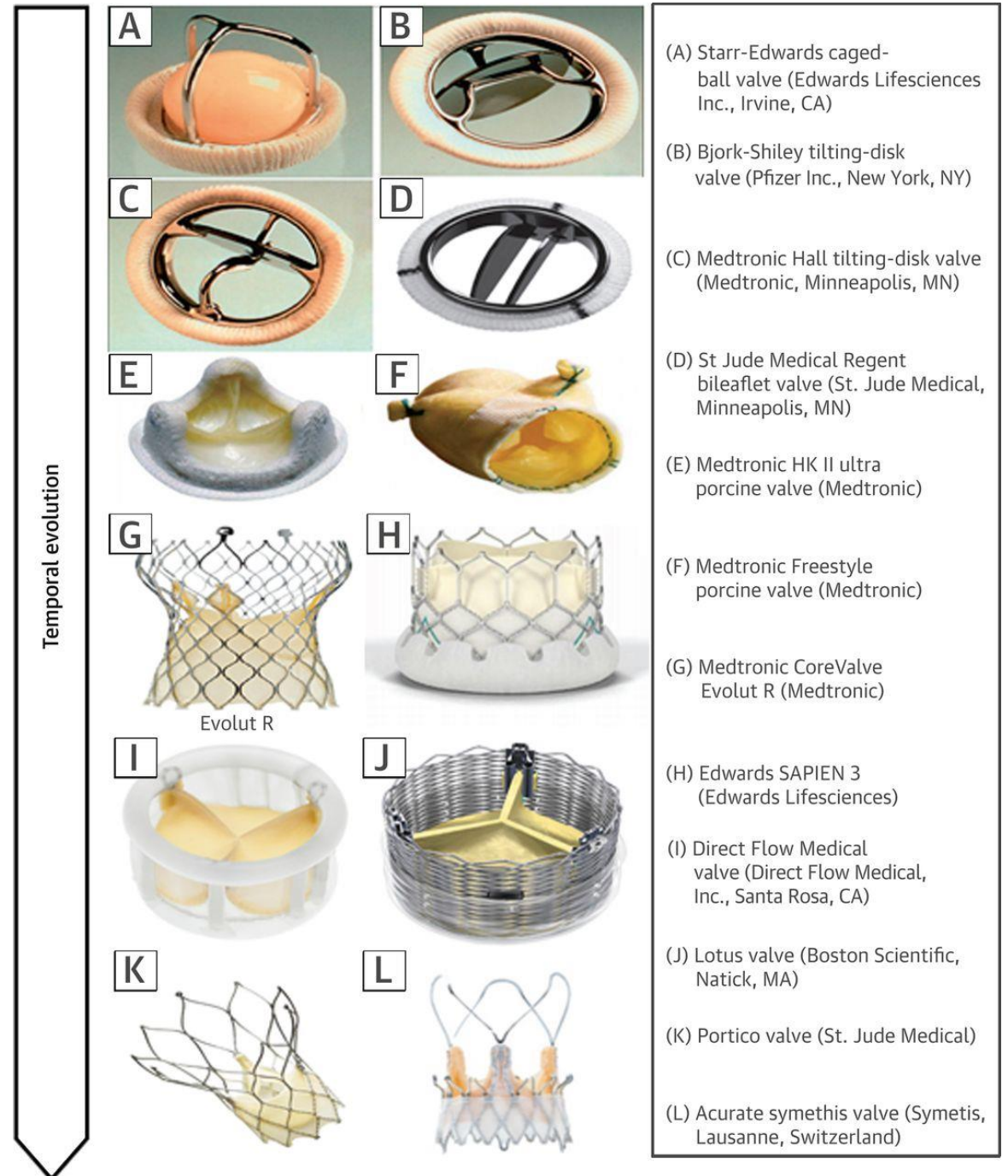
Basically two categories:

- Location
  - Aortic
  - Mitral
  - Tricuspid
- Type:
  - Mechanical
  - Bioprosthetic (Tissue)



# Heart Valves

- Anticoagulation is to prevent:
  - Thromboembolic events (similar to A. Fib)
  - Thrombosis of the valve itself (clot blocks the valve)
  - Subclinical organized thrombus which may impair long-term valve function (clot inhibits valve function)



Indication	Aortic	Mitral	Tricuspid
<b>Mechanical (caged ball, older generation tilting disk)†</b>	High risk – full anticoagulation  Typical INR range: 2.5-3.5	High risk – full anticoagulation Typical INR range: 2.5-3.5	High risk – full anticoagulation  Typical INR range: 2.5-3.5
<b>Mechanical (bileaflet, newer generation tilting disk) <u>with</u> additional risk factors (A. fib, previous thromboembolism, known hypercoagulable condition, left ventricular dysfunction)†</b>	High risk – full anticoagulation  Typical INR range: 2.5-3.5	High risk – full anticoagulation  Typical INR range: 2.5-3.5	High risk – full anticoagulation  Typical INR range: 2.5-3.5
<b>Mechanical (bileaflet, newer generation tilting disk) <u>without</u> additional risk factors†</b>	Low risk – may hold anticoagulation for short time, but still requires full anticoagulation Typical INR range: 2.0-3.0	High risk – full anticoagulation  Typical INR range: 2.5-3.5	High risk – full anticoagulation  Typical INR range: 2.5-3.5
<b>Mechanical On-X AVR†</b>	Low risk – depends on additional risk factors Typical INR range: 2.0-3.0 for 3 months, then 1.5-2.0	N/A	N/A
<b>Bioprosthetic (tissue) <u>with</u> additional risk factors (A. fib, previous thromboembolism, known hypercoagulable condition, left ventricular dysfunction)†</b>	Low risk – depends on additional risk factors  Typical INR range: 2.0-3.0	Low risk – depends on additional risk factors  Typical INR range: 2.0-3.0	Low risk – depends on additional risk factors  Typical INR range: 2.0-3.0
<b>Bioprosthetic (tissue) <u>without</u> additional risk factors†</b>	Very low risk – only anticoagulation for a short duration Typical INR range: 1.8-2.5*	Very low risk – only anticoagulation for a short duration Typical INR range: 1.8-2.5*	Very low risk – only anticoagulation for a short duration Typical INR range: 1.8-2.5*
<b>TransTAVR†</b>	Very low risk – reasonable to anticoagulate at least 3 months Typical INR range: 2.0-3.0	N/A	N/A

# Heart Valves

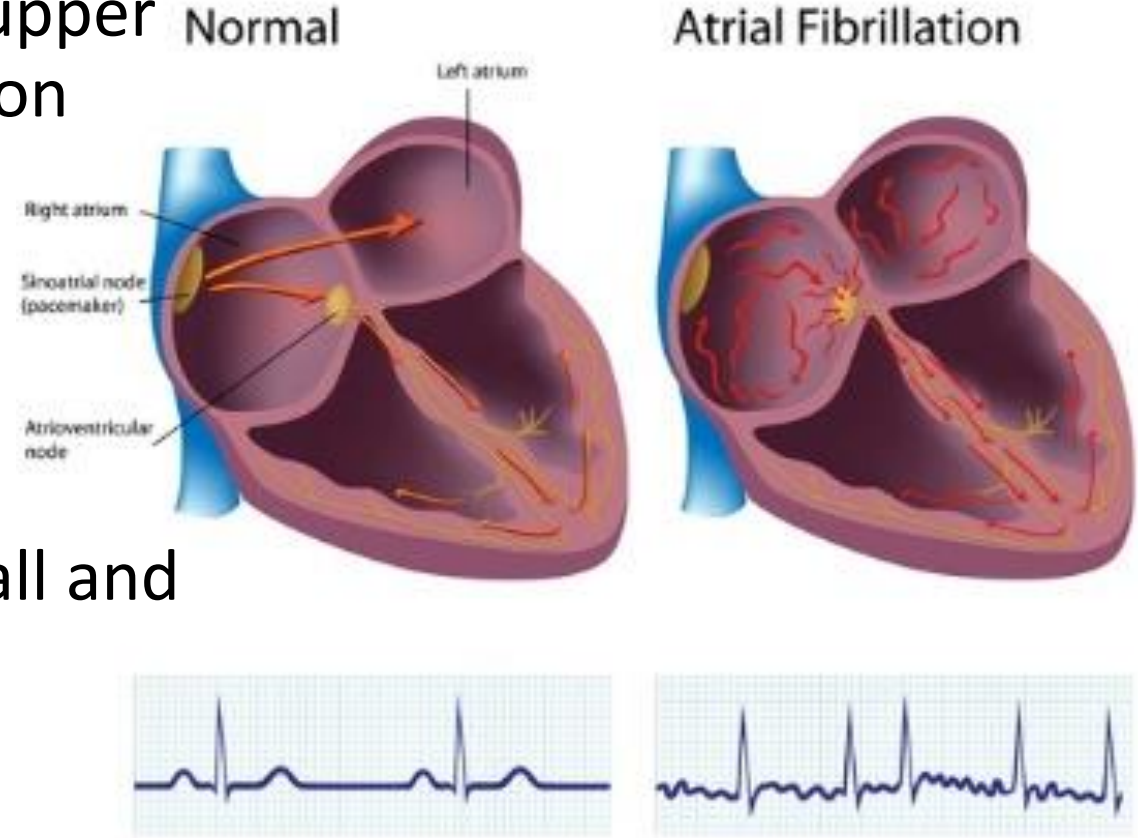
- Type and Duration of Anticoagulation:
  - If utilizing full anticoagulation – warfarin or enoxaparin (Lovenox)
    - Warfarin INR goal for high risk – 2.5 to 3.5
    - Warfarin INR goal of low to moderate – 2.0-3.0
    - Warfarin INR goal for OnX Valve in some patients – 1.5-2.0
  - Cannot utilize DOACs:
    - Dabigatran (Pradaxa) was found to actually increase risk of thromboembolism
    - Other DOACs do not have FDA indications for heart valve anticoagulation
  - If low risk, likely only aspirin for life – similar to stent placement

# Atrial Fibrillation



# Atrial Fibrillation

- Most likely to see – 2017 CDC Estimate: 2.7-6.1 million Americans
- Issues in signal conductivity leads to upper atriums of heart quivering or fibrillation
- Fibrillation leads to increased risk of coagulation cascade being activated
- Clot formed becomes potential thromboembolism
- Illustration for patients: Clot is baseball and heart is baseball pitching machine



# Atrial Fibrillation

- Destination of clot formed:
  - Highest concern is brain, resulting in ischemic stroke
  - Still high concern, but lower chance:
    - Lungs, resulting in pulmonary embolism – may be both consequence and cause of atrial fibrillation
    - Heart, resulting in myocardial infarct (MI)? – Debated at this point, appears a. fib. doubles risk of MI, however; contested if it causes it
- Valvular vs Non-valvular A. Fib.
  - Once a heart valve is part of the equation, risk of embolism increases
  - Newer agents are not approved for valvular atrial fibrillation

# Atrial Fibrillation

- Types: Paroxysmal, Persistent and Permanent

Paroxysmal	Persistent	Permanent
Terminates spontaneously, usually within 48 hours	Will not terminate spontaneously, but can be electrically cardioverted or converted with drugs	Will not terminate spontaneously, and is refractory to cardioversion

# Atrial Fibrillation

- Goals of Treatment:
  - Reduce risk of thromboembolism formation
  - Control Rhythm/Rate of the Heart – Either chemical or procedural
  - Reduce Pressures on Heart – Reducing the likelihood 1 & 2 will occur, reoccur or get worse
- Rhythm/Rate Control – Which is better? Still under debate (about same)
- Rhythm – pattern of heart beat (How often?) - Rate – Speed of heart beat (How fast?)

## **Rate Control Medications:**

- Beta blockers (metoprolol, carvedilol, atenolol)
- Nondihydropyridine Calcium-Channel Blockers (verapamil, diltiazem)
- Digoxin
- Amiodarone – interacts with everything

## **Rhythm Control Medications:**

- Amiodarone - interacts with everything
- Dofetilide - not started outside hospital
- Dronedarone
- Flecainide - “pill in pocket”
- Propafenone - “pill in pocket”
- Sotalol

# Atrial Fibrillation

More permanent treatment attempt options:

- Cardioversion:
  - Electrical
  - Chemical
- Ablation
- Surgery:
  - Pacemaker
  - Open-heart maze procedure

Controlling factors that pressure the heart:

- High blood pressure
- Diabetes
- Obesity
- Obstructive sleep apnea
- Smoking
- Alcohol use

# Atrial Fibrillation

- Anticoagulation:
  - Warfarin (most common) – typical INR goal 2.0 to 3.0
  - Any newer DOAC agent (preferred) – Non-valvular A. Fib nod over warfarin
  - Enoxaparin – Typically when warfarin therapy failed
  - Aspirin – May be appropriate for CHA2DS2-VASc score of 1 or less in men, or 2 or less in women

CHA2DS2-VASc Score

# CHA<sub>2</sub>DS<sub>2</sub>-VASc Score

## Scoring Differences Between CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc

Risk Factor	CHADS <sub>2</sub> (Maximum score, 6)	CHA <sub>2</sub> DS <sub>2</sub> -VASc (Maximum score, 9)
	Points	Points
<b>Congestive heart failure</b>	1	1
<b>Hypertension</b>	1	1
<b>Diabetes</b>	1	1
<b>Vascular disease</b>	N/A	1
<b>Age 65-74</b>	N/A	1
<b>Age ≥75</b>	1	2
<b>Female sex</b>	N/A	1
<b>Previous stroke/TIA</b>	2	2

*N/A – not applicable*



# CHA2DS2-VASc Score

- Only for Atrial Fibrillation risk calculation:
  - C – Congestive Heart Failure
    - No designation between preserved or reduced ejection fraction
  - H – Hypertension
  - A – Age
    - 65 to 74 y/o – 1 point
    - 75+ y/o – 2 points
  - D – Diabetes
  - S – Stroke or previous thromboembolism
  - V – Vascular disease (MI, atherosclerosis, stent, CAD, PAD)
  - A – Age (again – refer above)
  - Sc – Sex Category

# CHA<sub>2</sub>DS<sub>2</sub>-VASc Score

<b>CHA<sub>2</sub>DS<sub>2</sub>- VASc score</b>	<b>Patients (N=7,329)</b>	<b>Thromboembolism rate (95% confidence interval)</b>	<b>Adjusted stroke rate (%/year)</b>
0	1	0 (0–0)	0.0
1	422	0.46 (0.10–1.34)	1.3
2	1,230	0.78 (0.44–1.29)	2.2
3	1,730	1.16 (0.79–1.64)	3.2
4	1,718	1.43 (1.01–1.95)	4.0
5	1,159	2.42 (1.75–3.26)	6.7
6	679	3.54 (2.49–4.87)	9.8
7	294	3.44 (1.94–5.62)	9.6
8	82	2.41 (0.53–6.88)	6.7
9	14	5.47 (0.91–27.0)	15.2

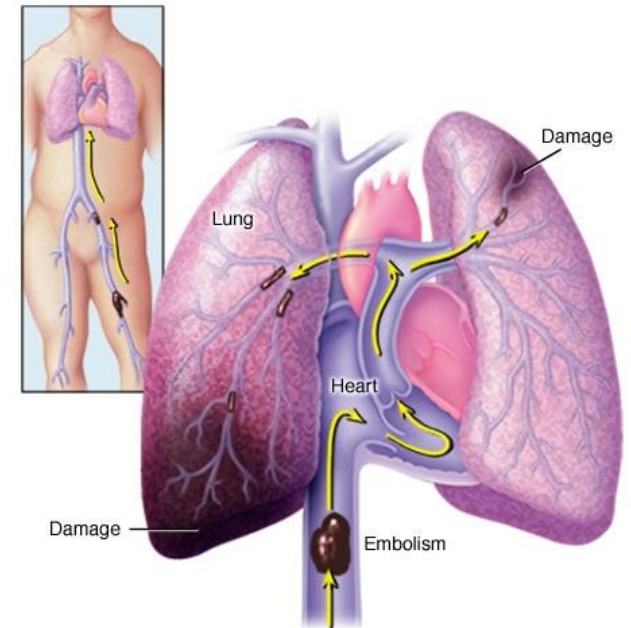
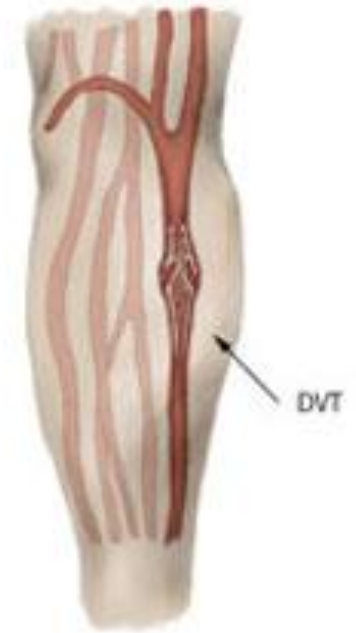
Thromboembolism(s)

# Thromboembolism(s)

Most common types:

- Deep Vein Thrombosis (DVT)
- Pulmonary Embolism (can be result of DVT)

May include embolism in any vasculature, but most common will be the venous system – occasionally see hepatic portal, renal system, upper arm venous return, etc...



# Thromboembolism

Treating the symptom, not the cause

Reasons for thromboembolism (hypercoagulable states):

- Hypercoagulable situations:
  - Provoked vs. Un-provoked
  - Risk factors:
    - Prolonged sedentary activity – lack of movement, obesity, conditions unable to move
    - Pregnancy or estrogen hormone replacement
    - Surgery (trauma)
    - Cancer
    - Venous catheter placement
- Antiphospholipid Syndrome (antiphospholipid antibodies)

# Thromboembolism

Reasons for thromboembolism (hypercoagulable states):

- Genetic (inherited) Variations:
  - Factor V Leiden mutation (heterozygous & homozygous)
  - Protein S or Protein C deficiency
  - Prothrombin Mutation (Factor II mutation)
  - Elevated Factor VIII levels
  - Antithrombin Deficiency

# Thromboembolism

## Anticoagulation agent:

- For most, any anticoagulant may be an option depending upon circumstance
- Exceptions where warfarin would be default choice:
  - Antiphospholipid syndrome
  - Other rarer – less studied

## Duration:

- Provoked – typically 3 to 6 months, then discussion of risk/benefits of coming off – would continue low dose aspirin indefinitely (30% risk reduction)
- Unprovoked – At least 3 to 6 months, then discussion of risk/benefits, encouragement for life long anticoagulation – if off, indefinite aspirin
- Inherited (genetic) condition – Until first embolism, likely none, then lifelong after

10 Minute Break



Agents for Anticoagulation:

Old and New

Anti-platelets

# Anti-platelets

## COX-1 Suicide Inhibitors (irreversible)

- Aspirin (acetylsalicylic acid)
  - Remember subsalicylates are part of this group (ex: Pepto Bismol)
  - Remember OTC ibuprofen, naproxen act similarly



## P2Y12 Inhibitors – blocks platelet adhesion by different means

- Clopidogrel (Plavix) - irreversible
- Ticagrelor (Brilenta) - reversible
- Prasugrel (Effient) - irreversible



# Aspirin Use

- Stent – If a stent has been utilized, it is already established the patient has cardiovascular disease, and thus evidence strongly supports indefinite use of aspirin for the prevention of new cardiovascular events. So unless there is a good clinical reason not to, the patient will be on aspirin for life for a stent. Dual antiplatelet therapy may be discontinued after 6 to 36 months, depending upon risk factors and tolerability of the patient, but if at all possible, aspirin (likely low dose) will be on for life.
- DVT/PE – Aspirin would be used in DVT/PE if the decision has been made to bring the patient off of warfarin (or other newer oral anticoagulant) after 3-6 months. In this case, the patient would be on the aspirin likely for life as it has shown a 30% reduction in recurrent DVT/PE.

Warfarin

# Warfarin (Coumadin, Jantoven)

- W – Wisconsin
- A – Alumni
- R – Research
- F – Foundation
- ARIN – from coumarin
- Rat poison? Yes!
  - Now: brodifacoum
- Vitamin K epoxide reductase inhibitor (Vitamin K plays role in synthesis of Factors II, VII, IX, X, Protein S & C)
- As indirect medication for anticoagulation there is a delay in effect based upon half-life duration of factors produced



# Anticoagulation – Warfarin Monitoring

- Monitoring – Prothrombin Time (PT) and International Normalization Ratio (INR)
- Typical range for INR 2.0-3.0 (may be higher or lower depending upon individual circumstances)
- Dose is very individualized – frequent changes



# Anticoagulation – Warfarin Reversal

- Vitamin K (from German/Scandinavian for Koagulation)
  - Found in higher amounts in darker green vegetables (also liver)
  - Vitamin K in diet is not contraindicated – importance of consistency
  - If control of warfarin is being problematic, consider starting a daily multivitamin with Vitamin K
  - Consider having a Vitamin K supplement on hand – if INR goes critical high (10+) and no bleeding is evident, may be quicker, easier and cheaper to get in system than prescription vitamin K:
    - 5 mg tablets of prescription Vitamin K is becoming quite expensive and pharmacies do not routinely carry it
    - Vitamin K is available as OTC supplement in 100 mcg (10 tablets = 1 mg)



# Anticoagulation – Why Warfarin?

- May be only anticoagulant approved for condition(s)
- Cost:
  - Warfarin is on \$4.00/\$10.00 generic lists – but must factor in laboratory costs
  - Most other newer anticoagulants are \$50-\$500 per month – especially on Medicare Part D plans, which does not allow use of Co-Pay cards
- Reversal agent is available in food and in supplements (as well as prescription tablets and injections)
- Large knowledge base regarding warfarin

# Heparin & Enoxaparin



Heparin

# Heparin (Unfractionated)

- What?:
  - Increasing the action of Antithrombin III which inactivates thrombin (Factor IIa) as well as Factor Xa
  - Dosed in units (IU) not in mgs – typical Sub-Q dose 5,000 IU every 8 hours
- Why?
  - Works well
  - IV administration makes easy to control and immediate onset of action
  - Half-life of 1-2 hours means out of system quickly (~8 hours)
  - Inexpensive
- Why not?
  - IV/Sub-Q administration invasive
  - Risk of HIT – Heparin Induced Thrombocytopenia

Enoxaparin (Lovenox)  
Dalteparin (Fragmin)  
Low Molecular Weight Heparin (LMWH)



# Enoxaparin (Lovenox)

- What?
  - Similar to Heparin, however; more so and longer against Factor Xa and less so against thrombin (Factor IIa)
  - About 1/4<sup>th</sup> size of Heparin on average
- Why?
  - Fast on/fast off anticoagulation:
    - 3-5 hours for effect after injection
    - About 6 hour half life – 4-5 half lives (about 24 hours) and out of system
  - Smaller molecule, reduced risk of HIT
  - Commonly used for “bridging”

# Enoxaparin (Lovenox)

- Why not?
  - Injection – some patients do not like this
  - Cost
  - Overbridging is common
- Dosing:
  - Must be dosed based upon renal function: Creatinine Clearance (CrCl) reported in mL/min:
    - $\text{CrCl (Male)} = ((140 - \text{age}) \times \text{weight in kg}) / (\text{serum creatinine} \times 72)$
    - $\text{CrCl (Female)} = \text{CrCl (Male)} \times 0.85$
  - Above 30 mL/min – 1 mg/kg twice daily or 1.5 mg/kg once daily
  - Below 30 mL/min – 1 mg/kg once daily (or 0.5 mg/kg twice daily – off label)
  - Post hip or knee arthroplasties: 30 mg twice daily or 40 mg once daily

# Dalteparin (Fragmin)

- What?
  - Dosed in units (IU) not mgs – typical SQ dose 5,000 IU once to twice daily
    - 2,500 IU of Anti-Factor Xa ~ 16 mg
  - Seemingly a little more usable in lower kidney disease
    - Accumulation not seen in severely ill patients with CrCl < 30 mL/min for 7 days
    - Caution still advised as primarily kidney cleared
  - Half-life 3-6 hours
- Why?
  - Possible medication shortage
- Why not?
  - Cost

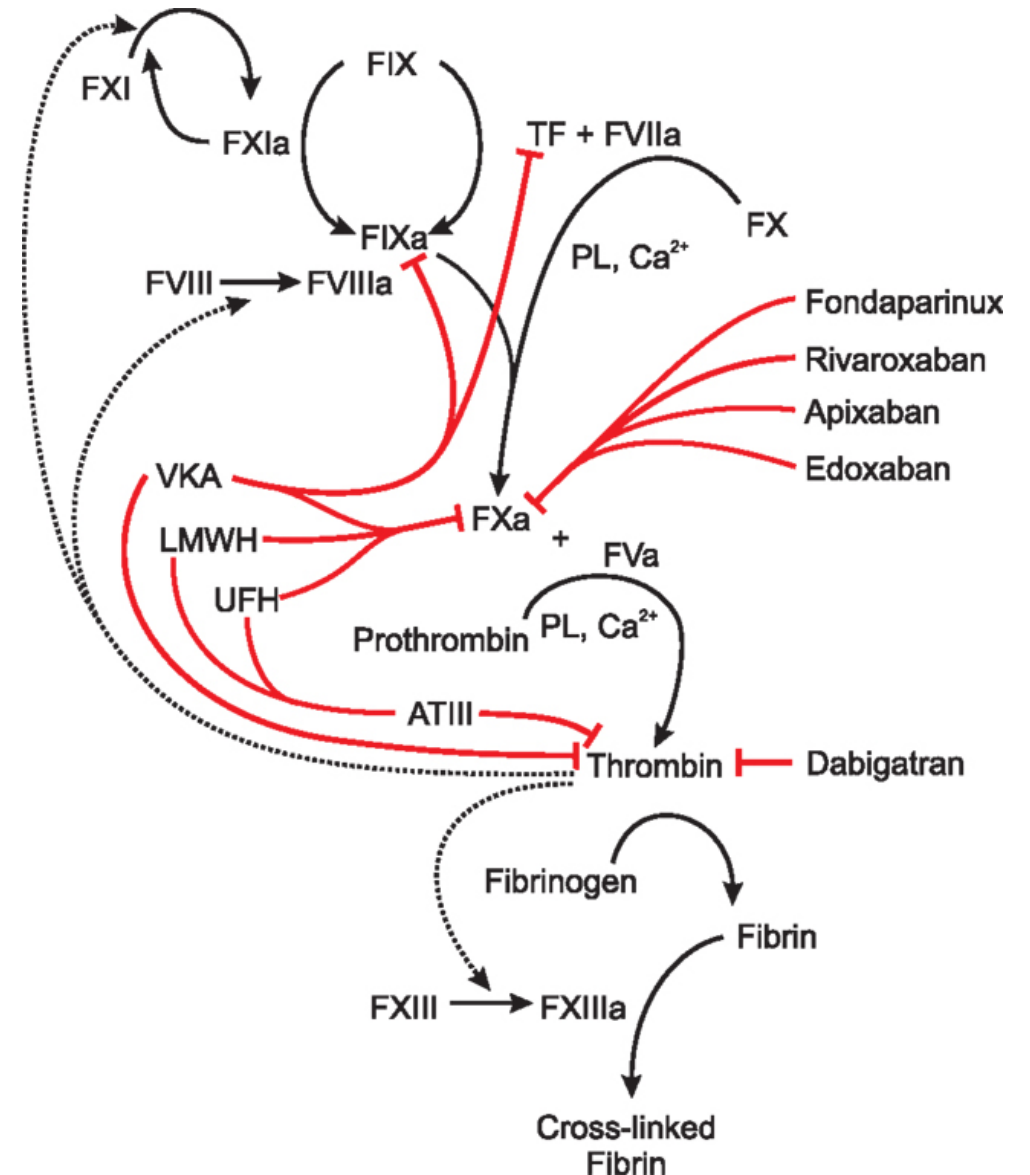


# Direct Oral Anticoagulants

Used to be called Novel Oral Anticoagulants - NOACs

# Direct Oral Anticoagulants

- Direct Thrombin Inhibitor
  - Dabigatran (Pradaxa)
- Activated Factor X Inhibitor (or Factor Xa Inhibitor)
  - Apixaban (Eliquis)
  - Rivaroxaban (Xarelto)
  - Edoxaban (Savaysa)
  - Betrixaban (Bevyxxa)
- Switching from/to warfarin
- Bridging with DOACs?



# Anticoagulation – dabigatran (Pradaxa)

- Direct Thrombin (Factor II) Inhibitor
- Typically 150 mg twice daily (may go 110 mg or 75 mg twice daily if other medications on board or bleeding risk)
- Monitoring – bleeding?
- Reversal Agent – Idarucizumab (Praxbind)



# Dabigatran (Pradaxa)

- What?
  - First DOAC approved
  - First to have reversal agent – Idarucizumab (Praxbind)
  - Included with other DOACs as preferred over warfarin in non-val. A. Fib
  - Increased thromboembolic occurrence with heart valve – study discontinued
  - Renal dosing – Not studied below CrCl 30 mL/min
  - Limited information in pregnancy
  - Limited time when opened to room ambiance
    - Not recommended to fill pill boxes
    - Open bottle only 4 months of use)
- Why? – Another option – dosing typically 150 mg twice daily
- Why not? – Above restrictions

# Anticoagulation – apixaban (Eliquis)

- Factor Xa Inhibitor
- Dosing typically 5 mg twice daily (10 mg for starting or 2.5 mg when bleeding risk)
- Monitoring – bleeding?
- Reversal Agent – Andexanet alfa (Andexxa)



# Apixaban (Eliquis)

- What?
  - Twice daily dosing Anti-Xa – typically 5 mg, may reduce to 2.5 mg
  - Renal dosing looks at serum creatinine levels (1.5 mg/dL), not CrCl
  - Need to look at weight:
    - > 120 kg or > 40 kg/m<sup>2</sup> is against ISTH 2016 guidelines – newer data seems to say ok rivaroxaban (Xarelto) slightly better
    - < 60 kg is considered in possible dose reduction
  - Need to look at age: > 80 y/o is considered in possible dose reduction
- Why?
  - By current analysis considered best DOAC for non-val. A. fib
    - Factors in benefit, adverse effects and cost
    - Not by a large margin – debatable
- Why not?
  - Cost
  - Heart valves – not demonstrated official benefit

# Anticoagulation – rivaroxaban (Xarelto)

- Factor Xa inhibitor
- Typically 15 to 20 mg once daily with food (2.5 mg twice daily for CAD)
- Monitoring – bleeding?
- Reversal Agent – Andexanet alfa (Andexxa)



# Rivaroxaban (Xarelto)

- What?
  - Once daily dosing Anti-FXa – Typical dosing 20 mg once daily
    - Other dosing:
      - 15 mg:
        - twice daily for treatment for 21 days, then switch to 20 mg once
        - Non-val. A. Fib and reduced kidney function (15-50 mL/min)
      - 10 mg once daily – for partial anticoagulation (ex: post TKA/THA) or PCI and non-val. A. fib.
      - 2.5 mg twice daily along with aspirin 81 mg once daily – CAD or PAD prevention of major cardio events
- Why?
  - Once daily dosing may be easier to remember (typically with biggest meal)
  - May be slightly better in obesity?
- Why not?
  - Cost or Mechanical heart valve



# Anticoagulation – edoxaban (Savaysa)

- Factor Xa Inhibitor
- Dosing typically 60 mg once daily (may go 30 mg if reduced kidney function)
- Monitoring – bleeding?
- Reversal Agent – Andexanet alfa (Andexxa)



# Edoxaban (Savaysa)

- What?
  - Once daily dosing Anti-Factor Xa – typical dosing 60 mg once daily
  - Must consider weight: < 60 kg, then 30 mg once daily
- Why?
  - Lower drug/drug interactions than other DOACs (minimal metabolism by CYP3A4 and predominate metabolite is active)
- Why not?
  - Kidney function too good – CrCl > 95 mL/min not recommended
  - Newest agent, may not be on formularies

# Anticoagulation – betrixaban (Bevyxxa)

- Factor Xa Inhibitor
- Dosing – Only currently approved for DVT prophylaxis for short duration (up to 42 days)
- Monitoring – bleeding?
- Reversal Agent – Andexanet alfa (Andexxa)



# Betrixaban (Bevyxxa)

- What?
  - Oral VTE prophylaxis agent for up to 42 days:
    - Typical dosing: 160 mg for one dose, then 80 mg daily
    - Renal impairment: CrCl 15 to 30 mL/min 80 mg for one dose, then 40 mg daily
- Why?
  - Another logical agent
- Why not?
  - Not indicated for longer than 42 days

# Other Anticoagulants

# Other Anticoagulants

- Fondaparinux (Arixtra)
  - Anti-Factor Xa
  - Half-life 15-17 hours: Stop 3-7 days prior to procedures

# Reversal Agents

- Fresh Frozen Plasma
- Vitamin K or 4 Factor Prothrombin Complex (Kcentra)
- Idarucizumab (Praxbind)
- Andexanet alpha (Andexxa)

# Summary – Main Points

- Blood is life – Coagulation and Anticoagulation are means to help address the system not functioning as it should
- Clots form in different parts of the vascular system and for different reasons, therefore the medications used to address them are different, although there is overlap
- Warfarin has been a gold standard of an anticoagulant, however; there are other agents, and DOACs are getting nod over warfarin in some conditions (atrial fibrillation)
- Although there are many different choices, continue to question if what you are on is best for you



*Thank  
You*

What Questions Do You Have?

Brian Barkow, PharmD, CSP, CDE