

# Thrombophilia

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# Objectives

- Define thrombophilia
- Describe causes
- Clinical presentations
- Use of investigations in thrombophilia
- Management of thrombophilia

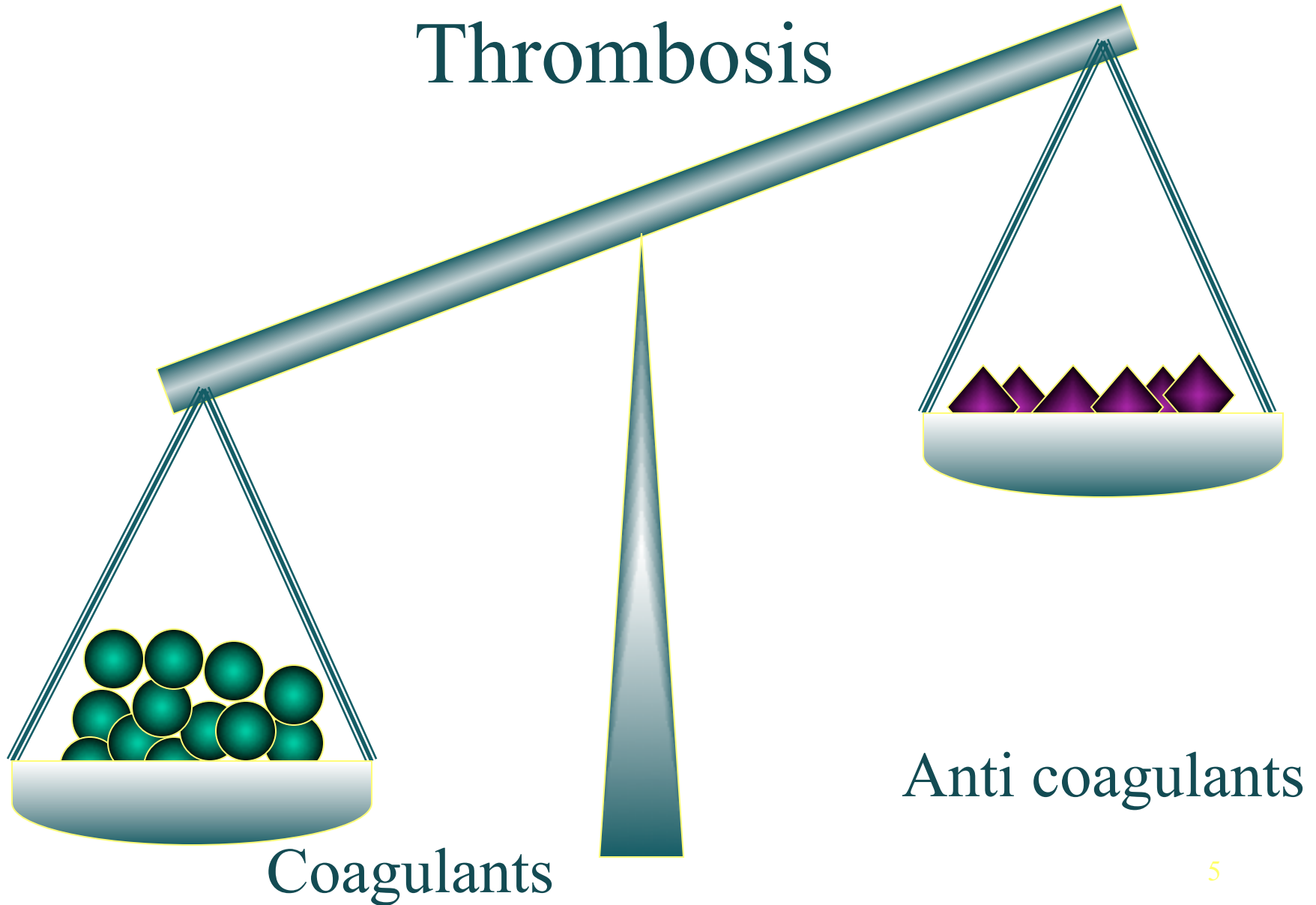
# Thrombophilia

Tendency to form  
blood clots within  
vessels

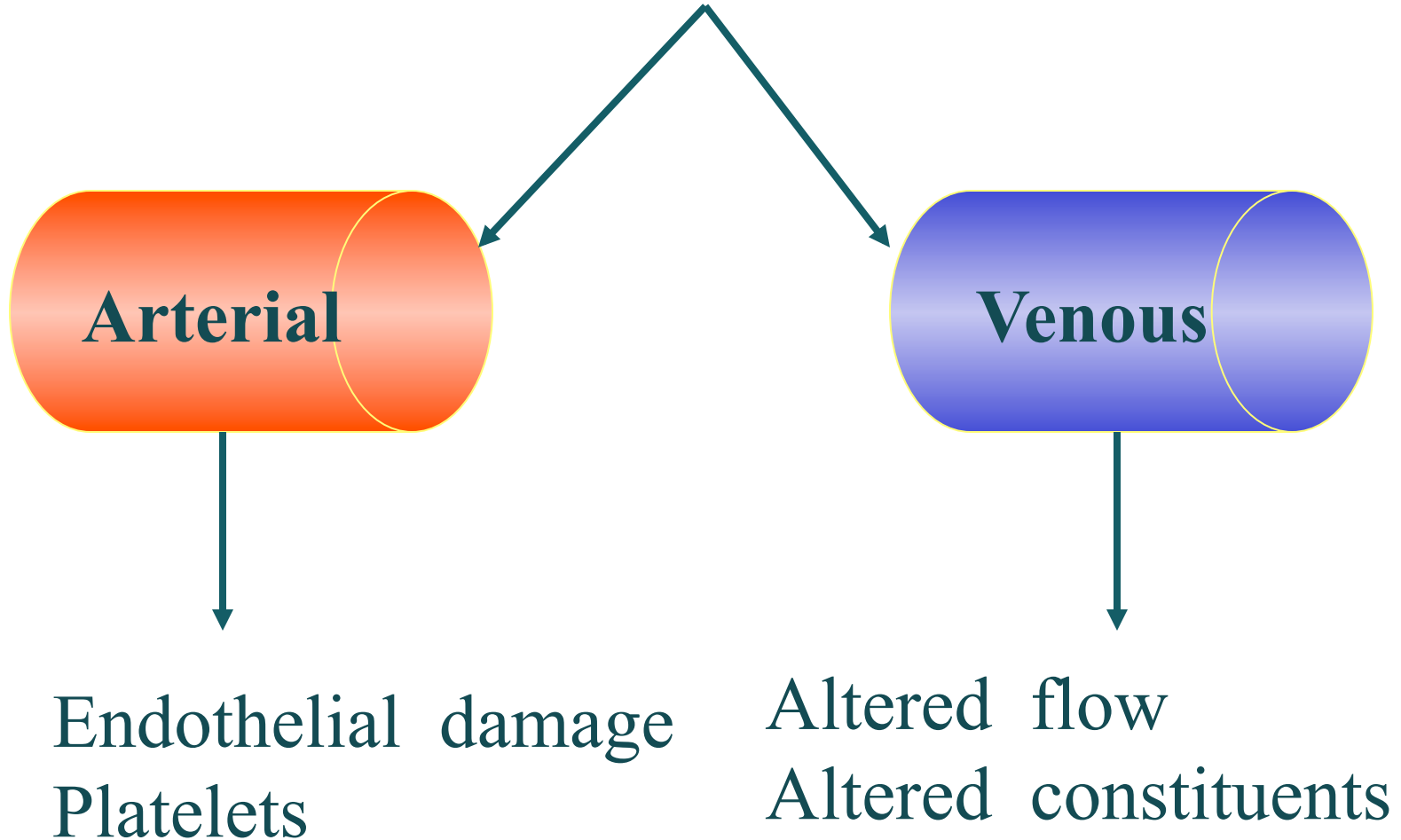
# Definition of a Thrombus

- Solid mass
- Formed in the circulation – vessels or heart
- From the constituents of the blood
- During life .

# Thrombosis



# Thrombosis



# Thrombophilia

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graph TD; Thrombophilia --> Acquired; Thrombophilia --> Inherited;
```

**Acquired**

*A*

**Inherited**

*I*

# Thrombosis

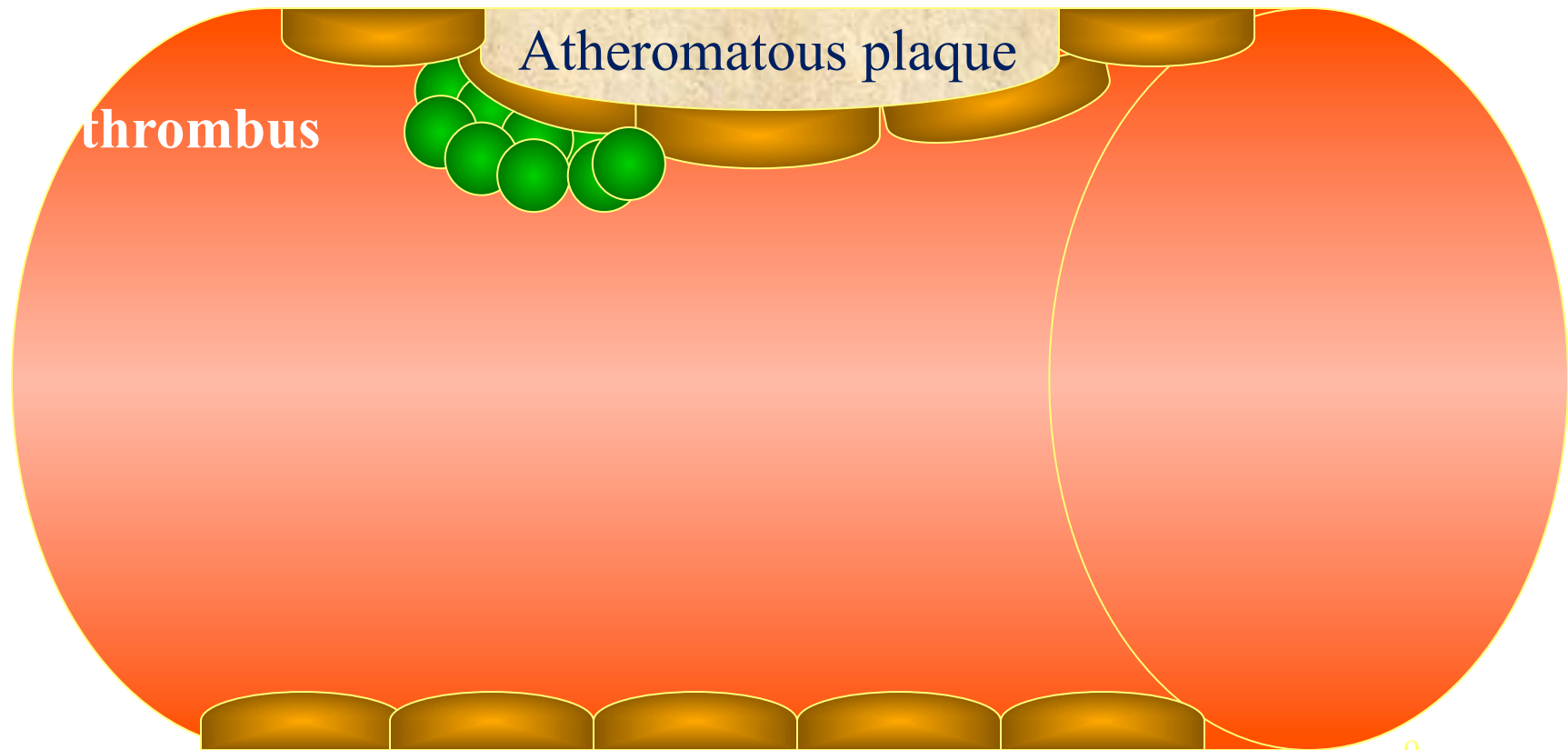
## Virchow's triad

- Endothelial cell damage
- Altered constituents of blood
- Altered flow within a vessel



# Pathogenesis of Arterial thrombi

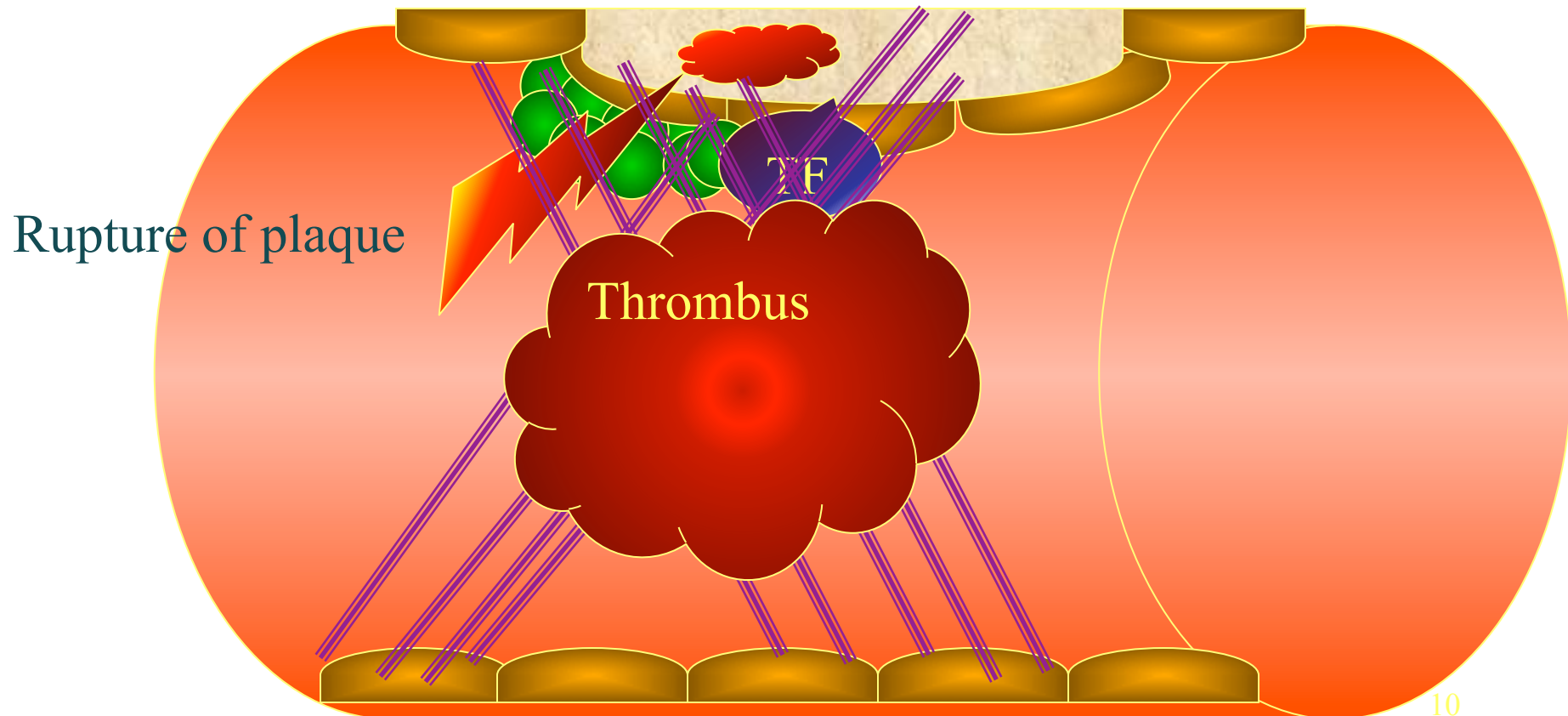
Endothelial cell injury



# Pathogenesis of Arterial thrombi

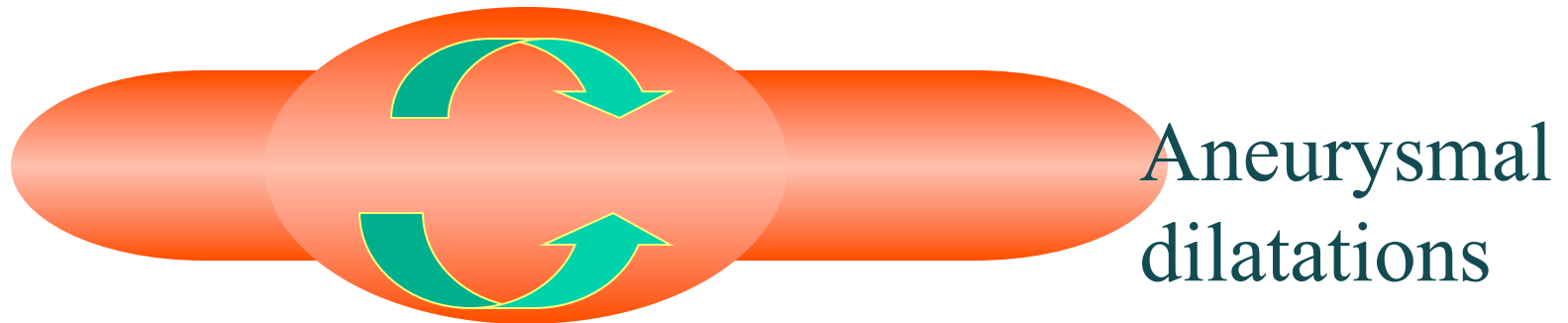
Endothelial cell injury

Haemorrhage into plaque



# Virchow's triad

## Altered flow within a vessel



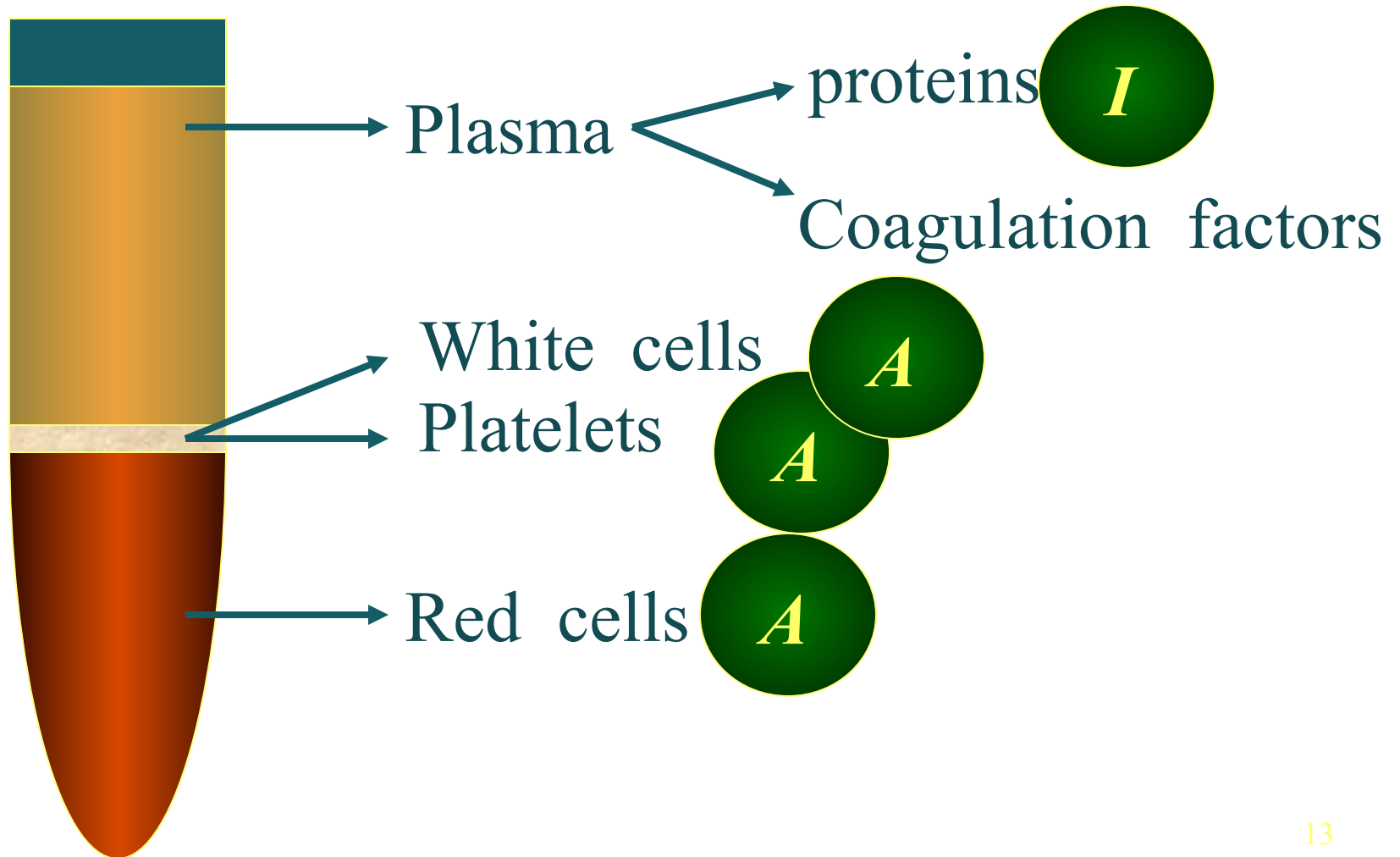
Coarctation /  
constrictions

# Venous thrombosis

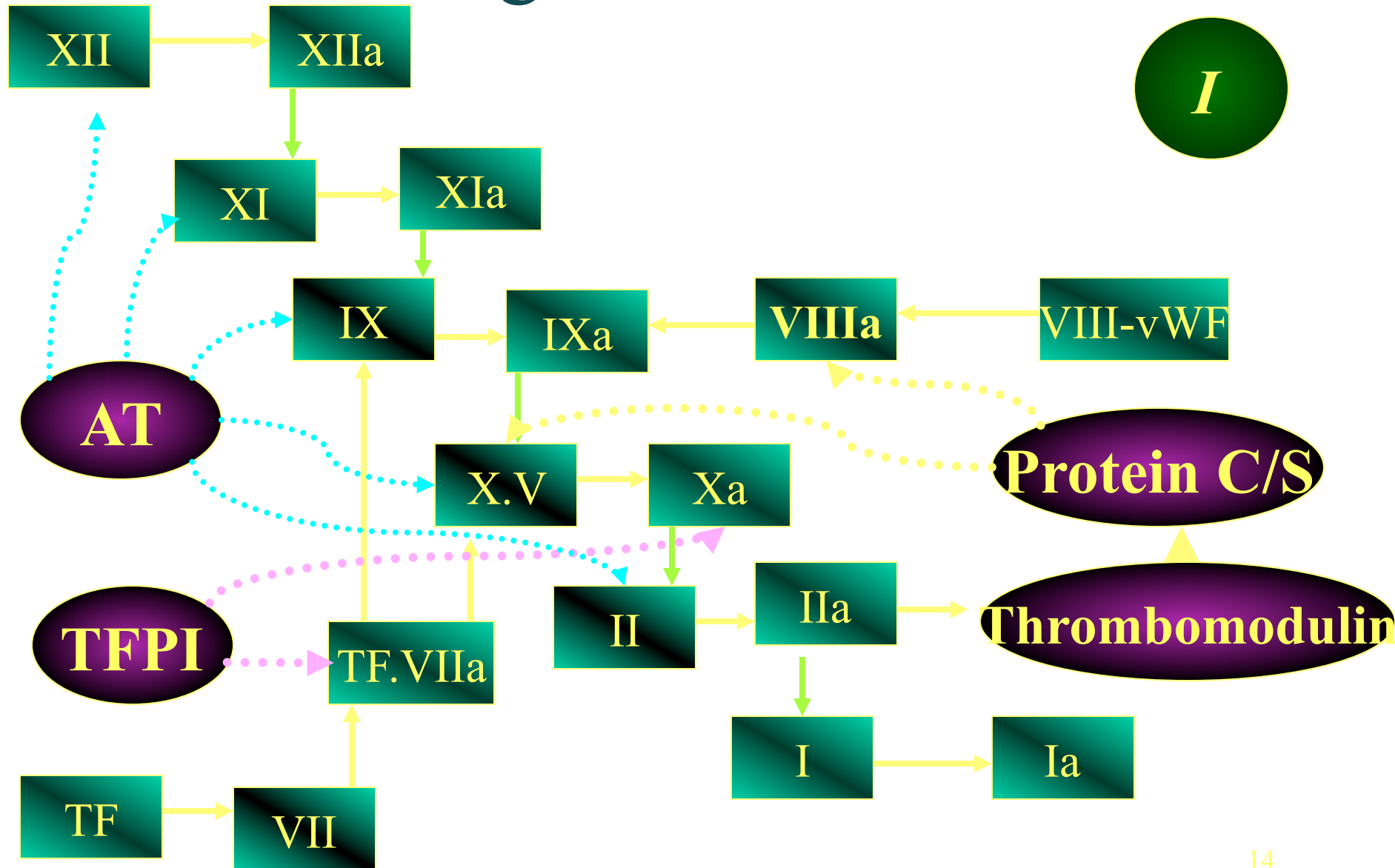
- Occurs in normal vessels
- Stasis
- Hypercoagulability
- ‘red thrombi’

# Virchow's triad

## Altered constituents of blood



# The Coagulation Cascade



# Thrombophilia

- Recurrent venous thrombosis
- Venous thrombosis < 40 years
- Unusual venous thrombosis
- Mesenteric
- Cerebral vein thrombosis
- Unexplained neonatal thrombosis
- Recurrent miscarriages
- Arterial thrombosis without arterial disease.

# Inherited causes of Thrombophilia

- Deficiency of an anti coagulant
- Protein C deficiency
- Protein S deficiency
- Anti thrombin deficiency
- Presence of a structurally abnormal procoagulant protein
- Prothrombin gene mutation
- Factor V Leiden
- Dysfibrinogenemia



# Protein C and S deficiency

- Autosomal dominant
- Increased risk of venous thrombosis < 40 yrs
- Homozygous protein C or S deficiency causes neonatal purpura fulminans
- Fatal without immediate replacement therapy.



# Antithrombin (AT) deficiency

- Autosomal dominant
- Acquired following trauma
- Major surgery
- Contraceptive pill
- Nephrotic syndrome
- Recurrent thrombotic episodes at a young age
- Relatively resistant to heparin

# Factor V Leiden

- Differs from normal factor V by a single nucleotide substitution (Arg506Gln)
- Is not cleaved by activated protein C
- Tendency to thrombosis
- 3–5% of population in the West
- Acts synergistically with acquired risk factors
- Pregnancy    OCPs

# Prothrombin variant A

- Also called G20210A
- There is elevated levels of prothrombin

# Homocysteine

- Both arterial thrombosis and venous thromboembolism.
- Occurs with folate and B12 deficiency
- Supplements helpful

# Investigations

- Full blood count including platelet count
- Coagulation screen
- Fibrinogen level
- Testing for specific causes of thrombophilia
- Assays for AT
- protein C
- protein S
- Assay for activated protein C resistance
- prothrombin variant
- Lupus anticoagulant

# Prevention & Treatment of Arterial thrombosis

- Anti platelet drugs
  - Aspirin
  - Dipyridamole
  - Clopidogrel
- Glycoprotein IIb/IIIa receptor antagonists
- Thrombolytic therapy - Streptokinase

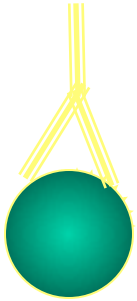
# Antiphospholipid syndrome

- Auto immune disorder
- Primary
- Secondary
  - - Systemic Lupus Erythematosus
  - - Infections
- Arterial or venous thrombosis and/or
- Recurrent miscarriages and
- Persistent antiphospholipid antibodies (aPL)

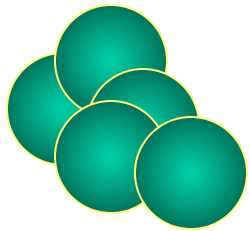


# Lupus anticoagulant

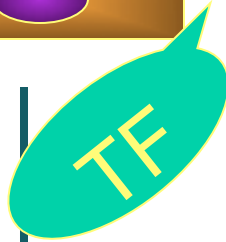
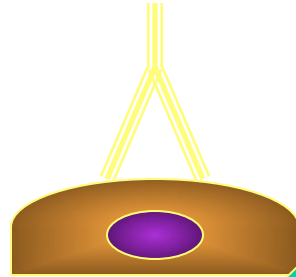
Platelet



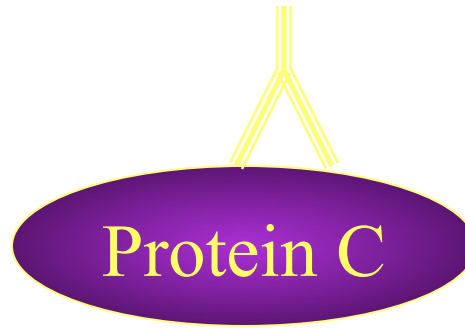
activation



Aggregation



Activation of  
coagulation  
pathways

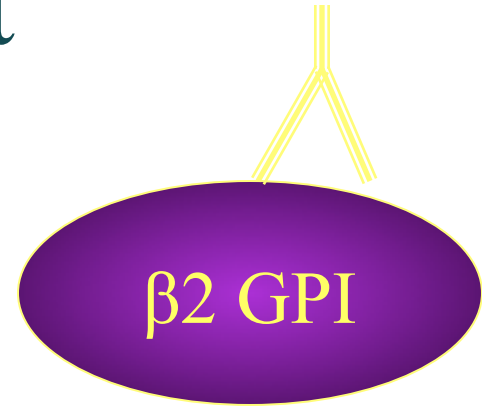
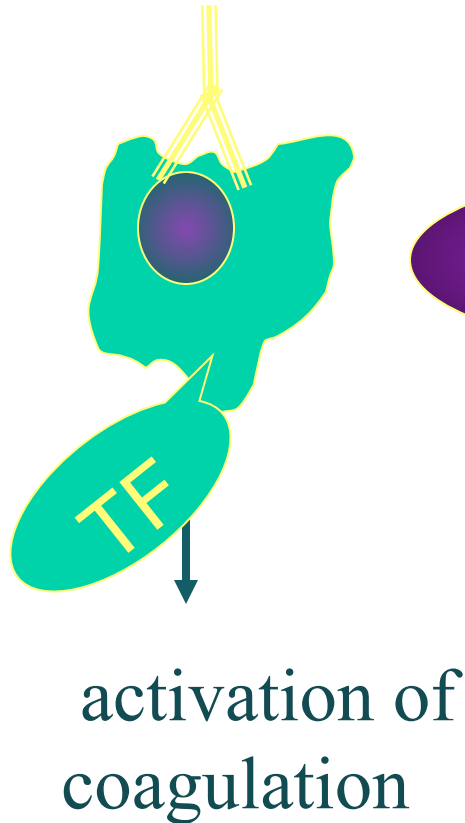


Deficiency leads to  
a pro coagulant  
state



# Lupus anticoagulant

Monocyte



# Clinical features

- Presence of thrombosis - arterial or venous
- Pregnancy loss
- Ischaemic stroke
- Thrombocytopenia
- Chorea
- Migraine
- Epilepsy
- Valvular heart disease
- Cutaneous manifestations - livedo reticularis
- Positive Coombs test
- Renal impairment

# Investigations

- The anticardiolipin test - detects antibodies IgG or IgM that bind cardiolipin
- Lupus anticoagulant test - anticoagulant effect in the test tube causes procoagulant effect inside the body
- Anti- $\beta$ 2-glycoprotein I test

# Catastrophic APS

- Rare
  - Multiple infarcts in different organs
  - Failure of multiple organs simultaneously
- High mortality

# Acquired causes of thrombophilia

# Acquired causes of thrombophilia

- Atherosclerosis
- Myeloproliferative disorders
- Paroxysmal nocturnal haemoglobinuria

