# Clinicopathological Case Conference of Haematological Medicine

## Episodes 5: Venous thromboembolism and preventable deaths

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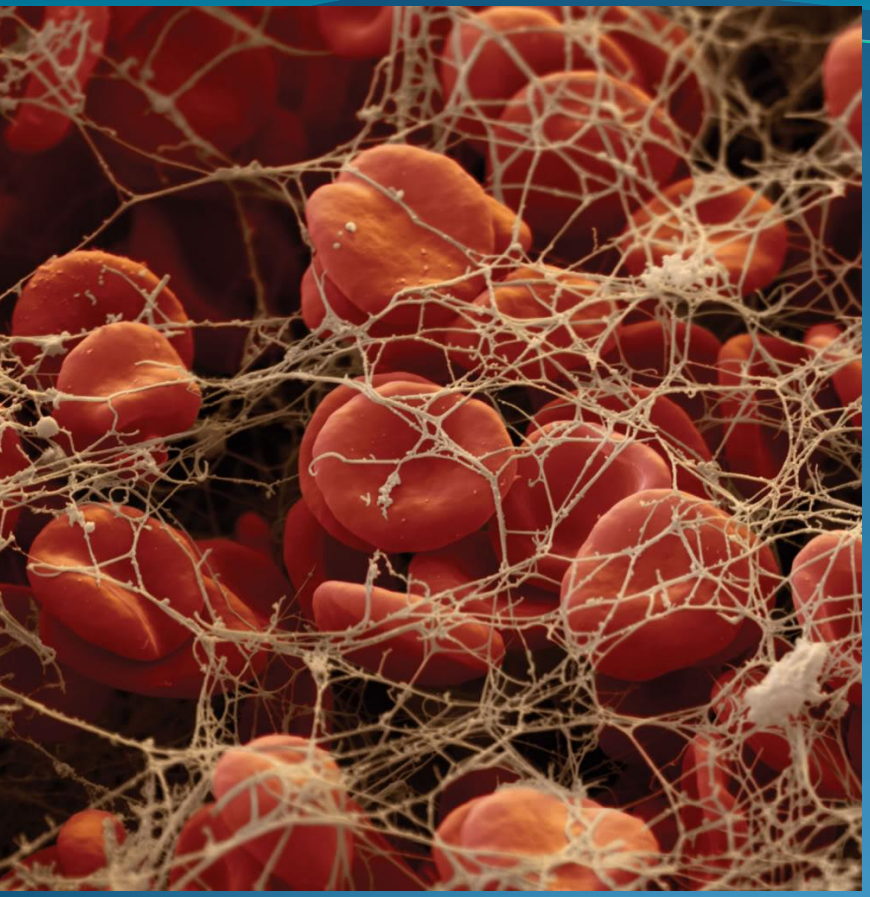


# VTE in malignancy and palliative care setting

# Background

- Cancer is associated with a 4 fold greater risk of thrombosis.
- Approximately 1 in 5 cancer patients develop a blood clot at some point in their lives.
- Occurrence of VTE has been proven to increase the likelihood of death in cancer patients by between two to six fold
- However, cancer patients are also associated with a higher annual risk of bleeding (13%) versus 4% in non-cancer patients.

# MOST COMMON CAUSES OF DEATH IN CANCER PATIENTS

- Sepsis
- **Thromboembolism**
- Organ failure
- Cachexia

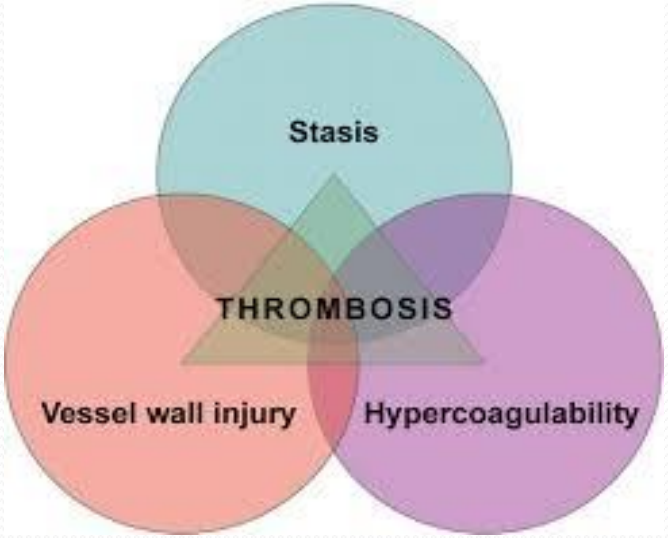
# Aims

- Why is there increased frequency of blood clots in cancer patients?
- Which agents are most effective for therapy and prophylaxis of VTE? Can we use NOACs?
- How long should we treat patients with VTEs for?
- Should we give high-risk cancer patients prophylactic treatment even in the absence of VTEs?

# Should we give prophylaxis to patients without known VTE?

- Recommendations for VTE prevention among hospitalised patients are clearly established.
- NCCN/ESMO/ACCP/USTH – suggest to evaluate the risks and benefits of thromboprophylaxis in ambulatory cancer patients.
- Nb for patients with multiple myeloma, the International Myeloma Working Group recommends prophylaxis with either LMWH or dose-adjusted warfarin for patients receiving lenalidomide or thalidomide-based combination regimens.

# 1. Why is there an increased VTE risk?

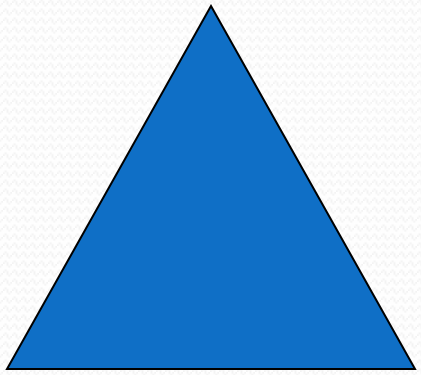



- Stasis of blood caused by tumour compression
- Vascular injury caused by intravasation of cancer cells, drug, or therapeutic devices
- Blood hypercoagulability due to the release of cancer cell proagulant factors

- The 3rd most common cardiovascular disorder
- Annual incidence 1-2 :1000 (<40y 1:10000, >80y 1:100)
- Affects 2-5 % of population during their lifetimes
- 20 % of patients with PE will die before diagnosis or on the first day
- PE mortality 30% without treatment , 2-8% with adequate treatment
- Long term complications: PTS (up to 40%) and chronic thromboembolic pulmonary hypertension (1-4%)
- Nearly two thirds of all VTE events result from hospitalization
- VTE is the single, most common, preventable cause of death in hospital patients
- More than 25000 deaths in the UK every year from preventable hospital acquired VTE (House of Commons Health Committee Report, 2005)
- Partly as a result of our ageing population and partly due to increased risk factors the number of cases DVT and PE is expected to rise

Virchow, R. (1856). "Thrombose und Embolie. Gefässentzündung und septische Infektion". *Gesammelte Abhandlungen zur wissenschaftlichen Medicin* (in German). Frankfurt am Main: Von Meidinger & Sohn. pp. 219–732.Matzdorff AC, Bell WR (1998). *Thrombosis and embolie (1846-1856).*

**endothelial injury**



**stasis of blood flow**

**hypercoagulability**

*Virchow's triad*

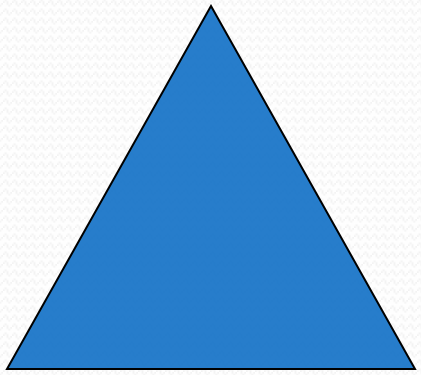
# VTE Pathogenesis

**Trauma or surgery**

**Heart valve disease or replacement**

**Indwelling catheters**

**AS**



**AF**

**Left ventricular dysfunction**

**Immobility or paralysis**

**Venous insufficiency, varicose veins**

**Venous obstruction**

**Malignancy**

**Pregnancy, peri-partum period**

**Oestrogen therapyl**

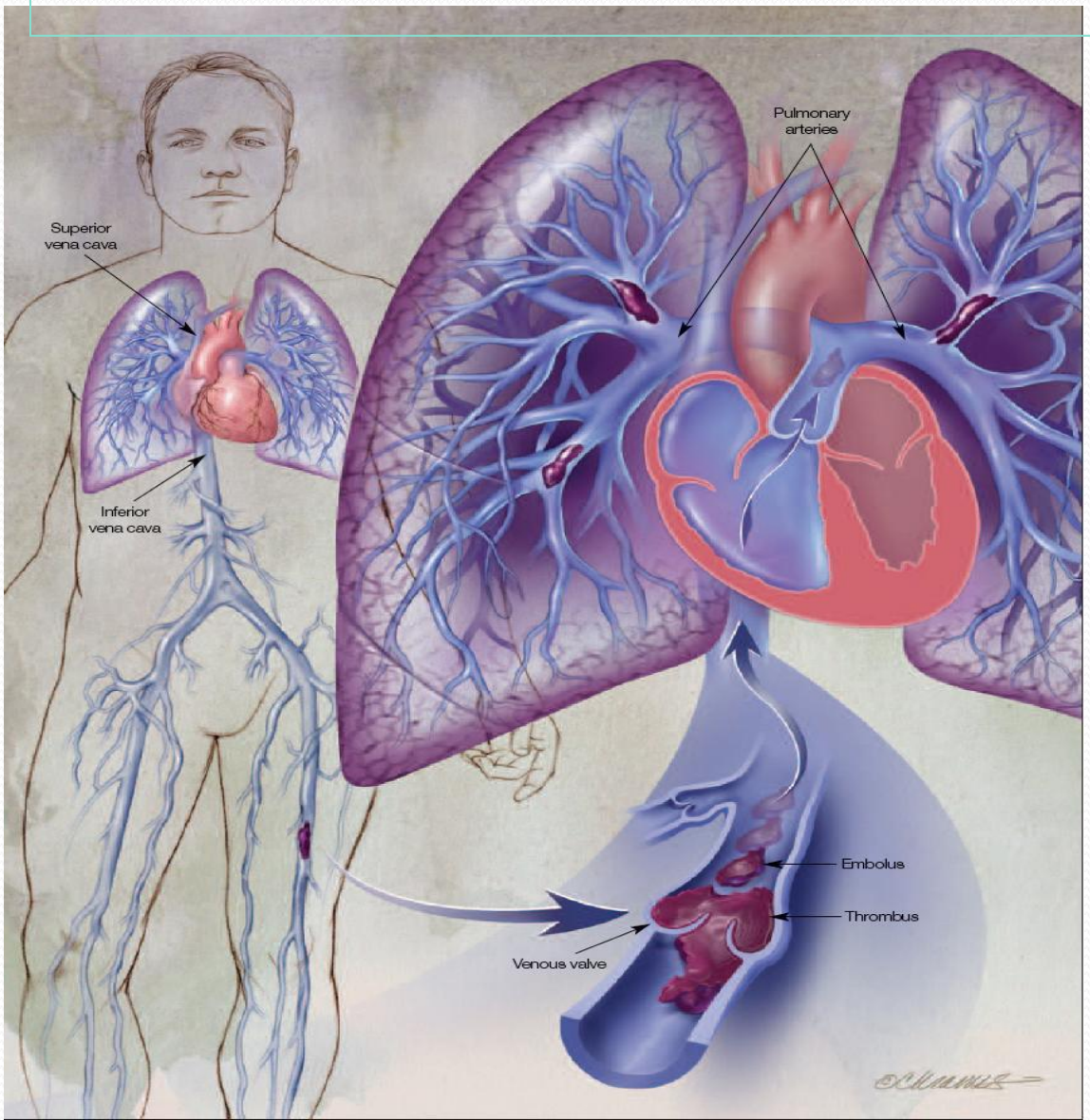
**Inflammatory bowel disease**

**Nephrotic syndrome**

**Sepsis**

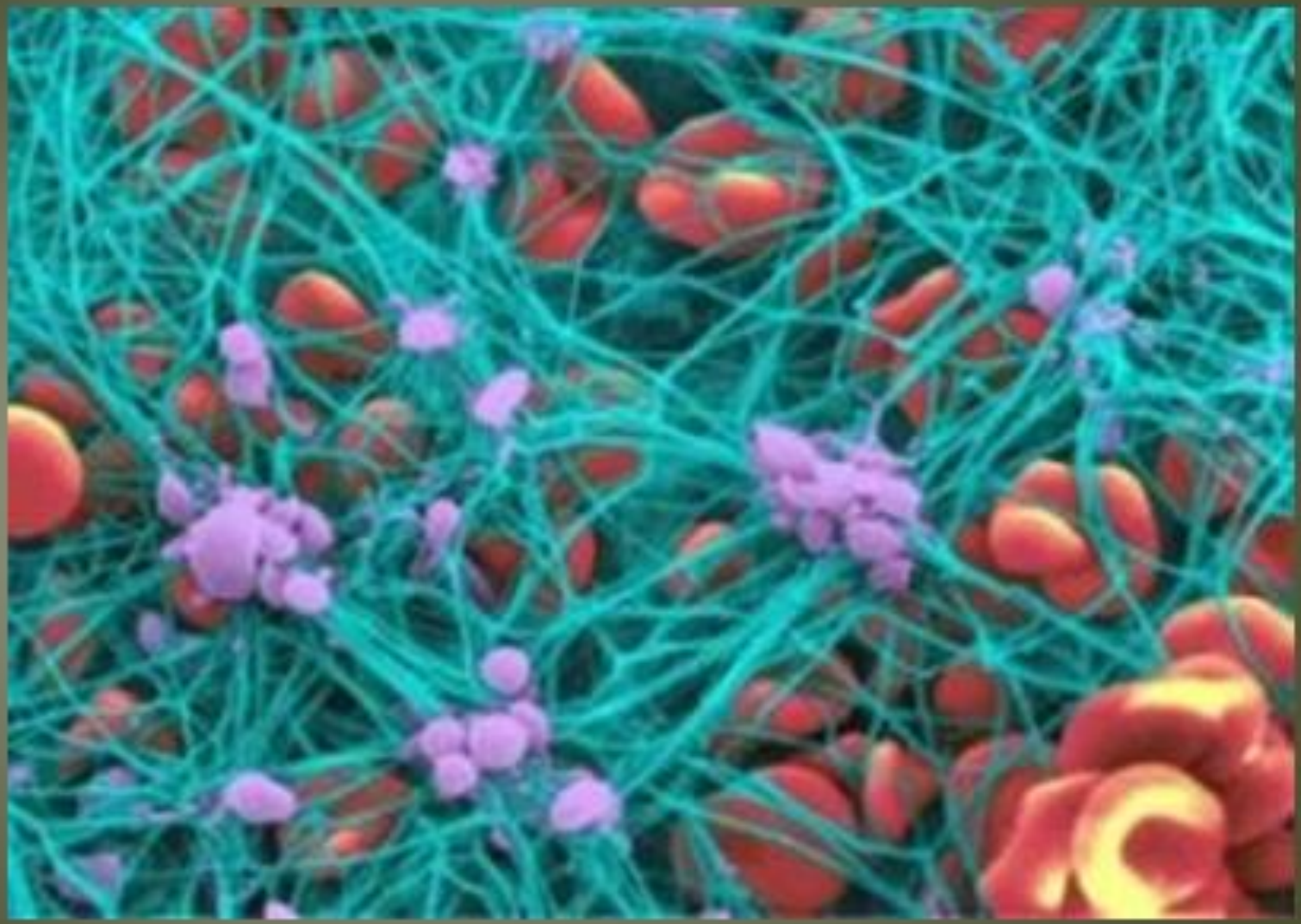
**Thrombophilia**

# VTE – pathophysiology




← PE

← DVT



# VTE Epidemiology

Presenting symptoms and signs are not specific

- Only 10-20% of patients investigated for DVT actually have the disease

- <u>DVT impersonators</u>

  - Cellulitis (6-9% probability)
  - Muscle injury (6-7%)
  - Superficial Thrombosis (6-7%)
  - Chronic Oedema or Venous Insufficiency (5-7%)
  - Pelvic tumours compressing lymphatic or venous drainage (1%)
  - Ruptured Baker's cyst (3%)

# VTE Epidemiology

- PE presentation is extremely varied and vague
- PE suspected when dyspnoea, pleuritic chest pain
- Massive PE ? ---syncope, collapse
- PE involving segmental or subsegmental arteries ?---minimal or no symptoms

# PE impersonators

Common causes of dyspnoea: (PE – 2%)

- asthma (33%)
- heart failure (31%)
- COPD (9%)
- arrhythmia (7%)
- infection (5%)
- interstitial lung disease (4%)
- Anaemia (2%)

Common causes of pleuritic pain (PE –18%)

- viral or idiopathic (46%)
- pneumonia (8%)
- chest wall trauma /cancer/other (25%)

# Clinical prediction tools for VTE diagnosis

## *Deep vein thrombosis (DVT)*

**Table 1 Two-level DVT Wells score[a]**

| *Clinical feature* | *Points* |
|---|---|
| Active cancer (treatment ongoing, within 6 months, or palliative) | 1 |
| Paralysis, paresis or recent plaster immobilisation of the lower extremities | 1 |
| Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia | 1 |
| Localised tenderness along the distribution of the deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swelling at least 3 cm larger than asymptomatic side | 1 |
| Pitting oedema confined to the symptomatic leg | 1 |
| Collateral superficial veins (non-varicose) | 1 |
| Previously documented DVT | 1 |
| An alternative diagnosis is at least as likely as DVT | −2 |
| ***Clinical probability simplified score*** | |
| **DVT likely** | **2 points or more** |
| **DVT unlikely** | **1 point or less** |

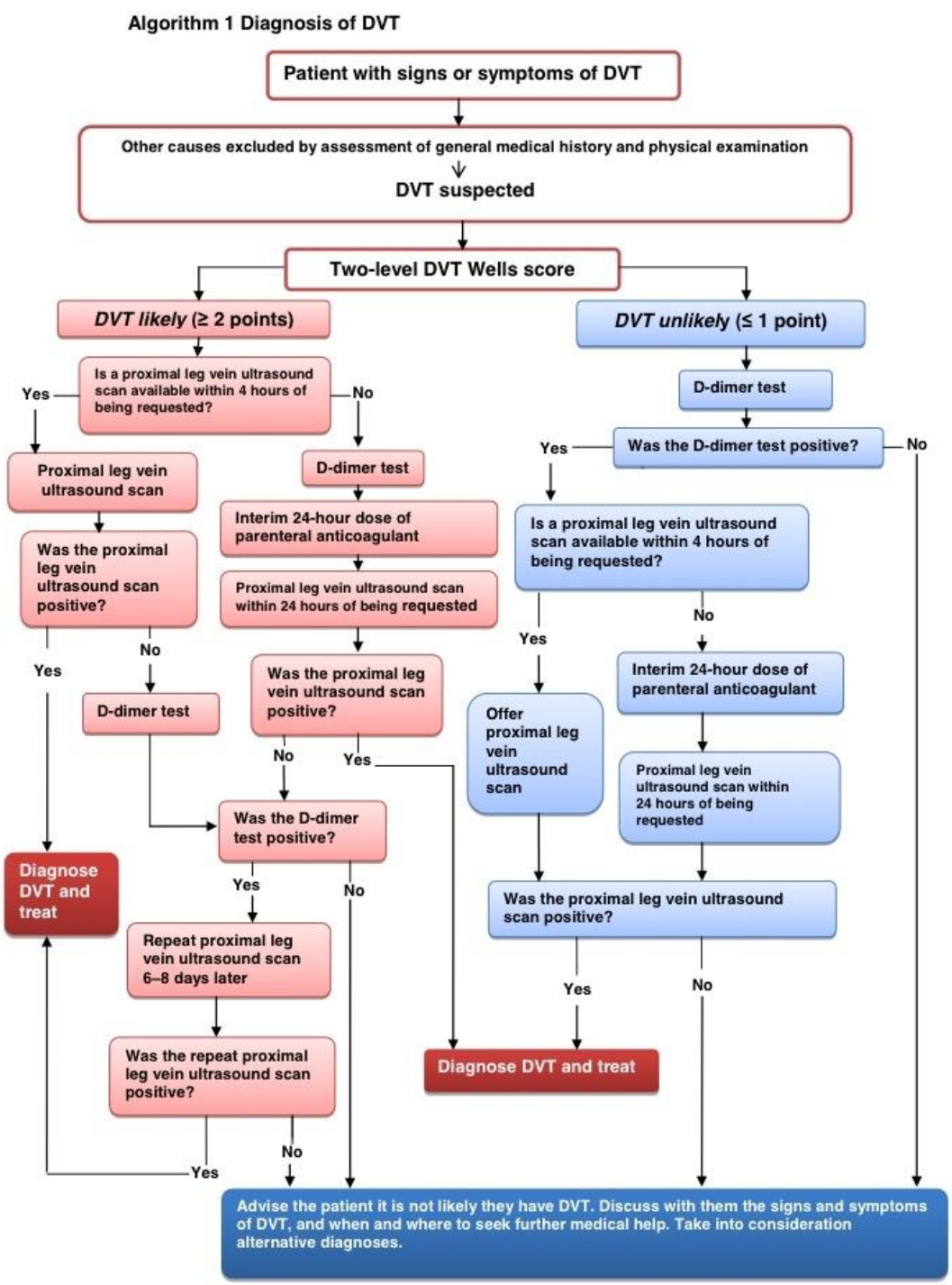
[a] Adapted with permission from Wells PS et al. (2003) Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis.

## Pulmonary embolism (PE)

**Table 2 Two-level PE Wells score[a]**

| *Clinical feature* | *Points* |
|---|---|
| Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins) | 3 |
| An alternative diagnosis is less likely than PE | 3 |
| Heart rate > 100 beats per minute | 1.5 |
| Immobilisation for more than 3 days or surgery in the previous 4 weeks | 1.5 |
| Previous DVT/PE | 1.5 |
| Haemoptysis | 1 |
| Malignancy (on treatment, treated in the last 6 months, or palliative) | 1 |
| ***Clinical probability simplified score*** | |
| **PE likely** | **More than 4 points** |
| **PE unlikely** | **4 points or less** |

[a] Adapted with permission from Wells PS et al. (2000) Derivation of a simple clinical model to categorize patients' probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer. Thrombosis and Haemostasis 83: 416–20




- **NICE guidance [CG144]**

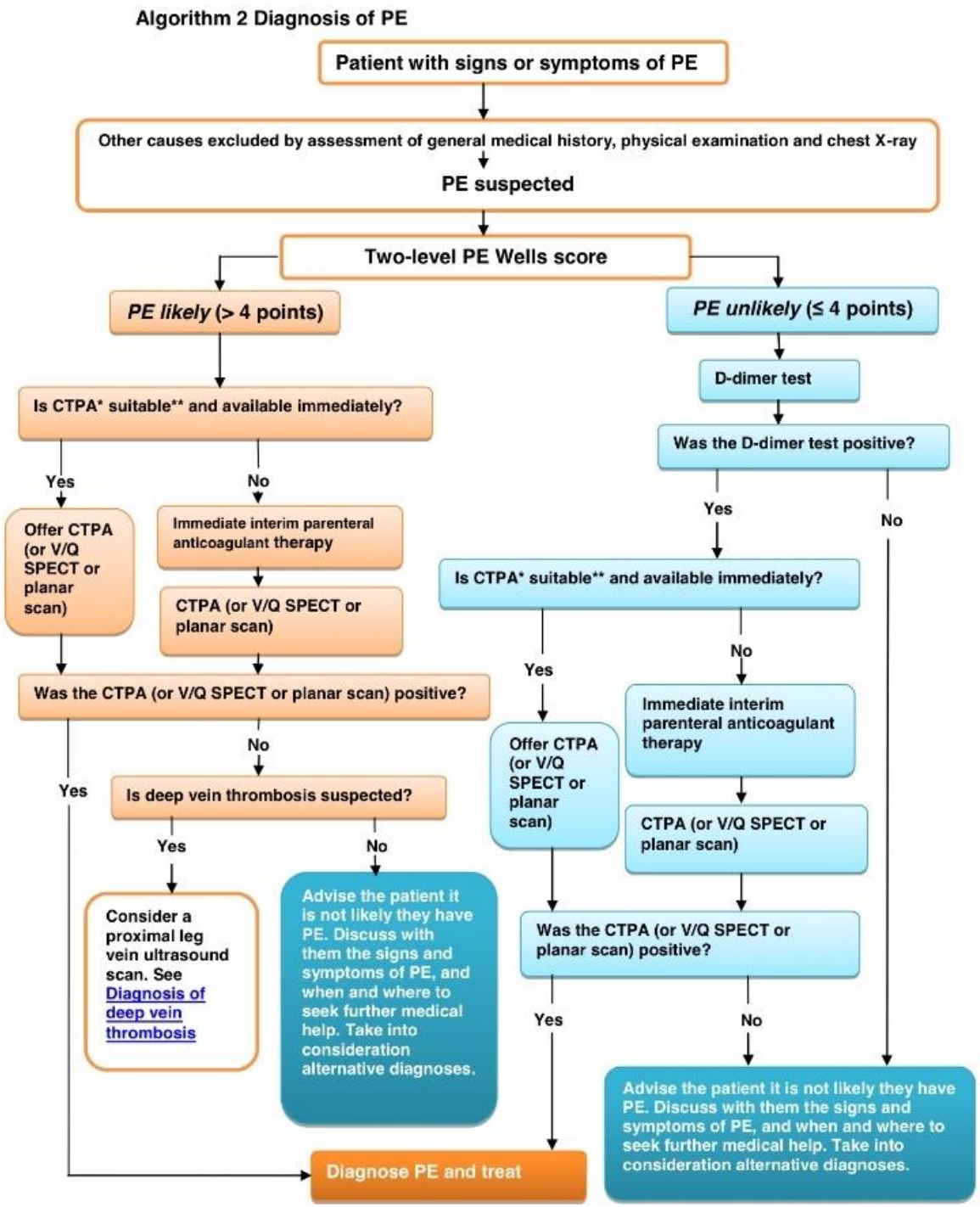
Published date: June 2012

Objective diagnosis of DVT depends on diagnostic imaging (proximal leg US scan)

Patients with low pretest probability **and** negative D-dimer can have DVT excluded without need for imaging

<u>D-dimer test</u>

-93-95% sensitivity
- 44-46% specificity
*Threshold for positive result is determined locally*




- **NICE guidance [CG144]**

Published date: June 2012

CTPA — *Imaging test of choice for PE diagnosis*

**Allergy to contrast**
**Renal impairment**
**Risk from irradiation is high**

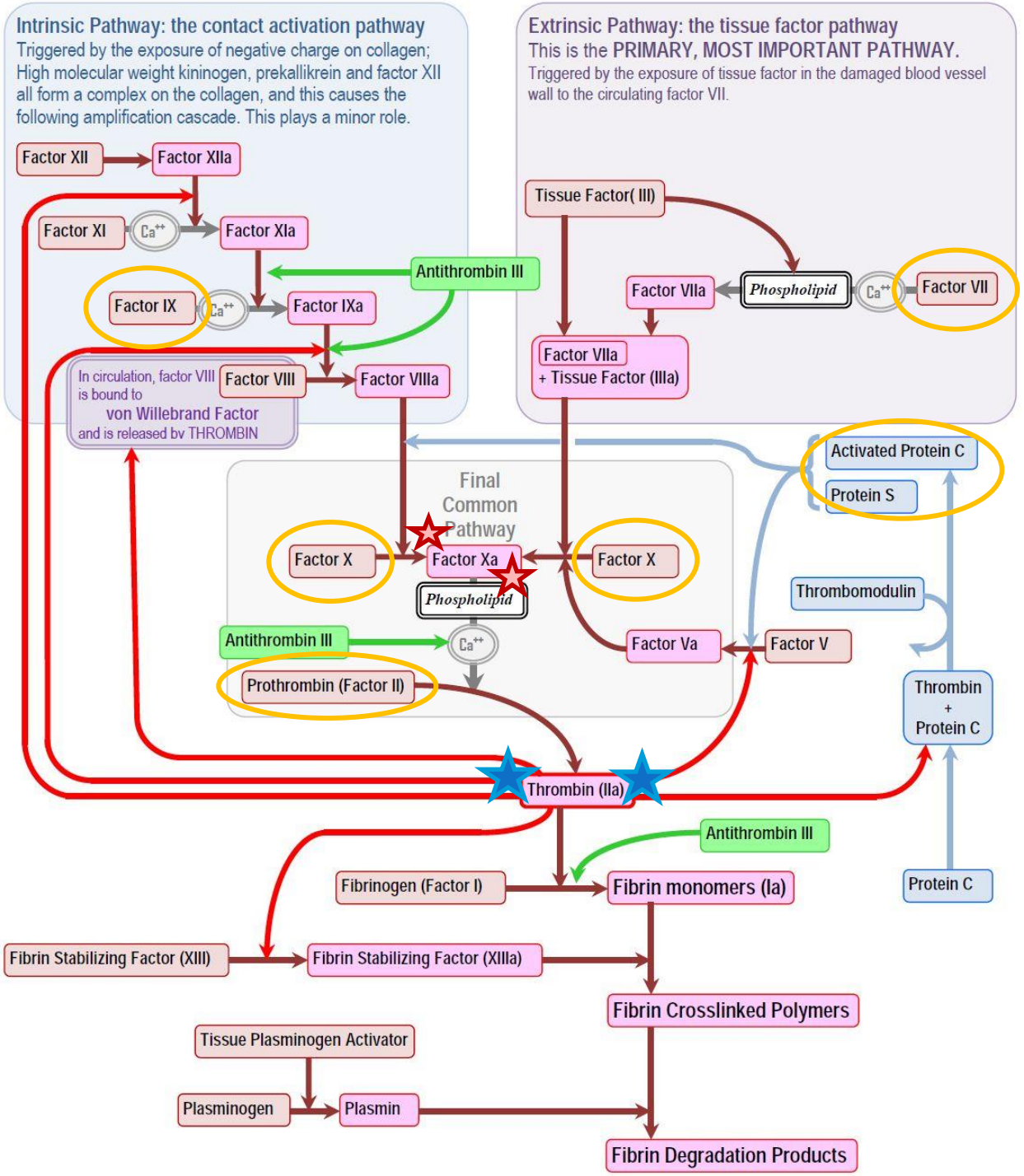
**V/Q spect scan**
**V/Q planar scan**

Patients with low pretest probability **and** negative D-dimer can have PE excluded without need for imaging

# VTE MANAGEMENT

- Anticoagulants are the cornerstone of VTE treatment

- Goal:
  - Prevent propagation of thrombus
  - Relieve symptoms
  - Prevent recurrent events




## Anticoagulants

= Depleted by VKAs

= Heparins:
UFH (all factors)
LMWH (mostly Xa)
Fondaparinux (Xa)

= Heparinoids
Danaparoid
Oral anti-Xa:
Rivaroxaban
Apixaban etc

= Direct thrombin inh.
Dabigatran
Argatroban

# VTE MANAGEMENT

| | |
|---|---|
| Initial phase (5-7d) | Rapidly acting parenteral anticoagulant (LMWH / UFH/ Fondaparinux) *overlapped* with VKA<br>*or* rivaroxaban (?other NOACs) |
| Long term phase (7d-3m) | VKA / rivaroxaban / ? NOAC |
| Extended phase (> 3-6 months) | VKA / rivaroxaban / ? NOAC |

# VTE MANAGEMENT

**LMWH**

- Current standard for initial VTE treatment
- 200u/kg, 120u/kg if GFR<10-20ml/min (unlicenced)
- SC, once daily, weight adjusted dose
- Until INR from concomitant VKA is therapeutic

*(at least 5 days or until INR >2 for at least 24h, whichever is longer)*

- PE with haemodynamic instability
- Increased risk of bleeding

⟶ UFH

Creatinine clearance < 30 ml/min

→ LMWH (antiXa monitoring) *or*

→ UFH (APTT monitoring)

NICE CG144

# VTE MANAGEMENT

**VKA**

- Target INR 2.5 (range 2-3)
- VTE on warfarin? Limited evidence to suggest target INR 3.5 (3-4)
- Load with 5 mg (5-5-5-INR)

**LMWH**

Cancer patients (labile INRs, drug interactions)
150u/kg sc od from month 2 onwards

**NOACs**

- Fast acting, no need for bridging with LMWH
- Possible all- oral treatment
- Replicable dosing effect, monitoring NOT required
- Rivaroxaban 15mg bd for 3 weeks→ 20mg od, no dose adjustments
- Dabigatran 150 mg bd
- Apixaban 10mg bd for 7 days → 5 mg bd

# VTE MANAGEMENT: Intermediate

NICE

CG144

Consider catheter directed thrombolysis for patients with symptomatic iliofemoral DVT + :

- Symptoms >14 days
- Good functional status
- Low risk of bleeding
- >1 year life expectancy

Consider pharmacological thrombolysis in patients with PE and haemodynamic instability, do not offer to patients with PE and haemodynamic stability

? PE + haemodynamic stability + right ventricular dysfunction ??

# VTE MANAGEMENT

## Temporary inferior vena caval filters

NICE CG144

Offer to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment.

Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:

- **increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy *or* switching treatment to LMWH**

Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly

# VTE MANAGEMENT

## Outpatient management of DVT

- Safe and effective in most patients
- Improved quality of life, cost savings

*Admit the following patients:*

- Co- existent serious medical pathology
- Severe acute venous obstruction
- Patients in significant pain
- Renal impairment creatinine > 200 µmol/l
- Liver disease
- Communication problems
- Poor social background
- Limited mobility
- Active bleeding
- High risk of bleeding

# Outpatient management of PE

**NICE CG144**

**Evidence update 55**

**Selected patients who are at low risk of adverse effects could safely receive anticoagulation on an outpatient basis or be discharged within 3 days**

**PESI or sPESI could be used to select**

**Table 1. Original and Simplified Pulmonary Embolism Severity Index (PESI)**

| Variable | Score: Original PESI[a] | Score: Simplified PESI[b] |
|---|---|---|
| Age >80 y | Age in years | 1 |
| Male sex | +10 | |
| History of cancer | +30 | 1 |
| History of heart failure | +10 | 1[c] |
| History of chronic lung disease | +10 | |
| Pulse ≥110 beats/min | +20 | 1 |
| Systolic blood pressure <100 mm Hg | +30 | 1 |
| Respiratory rate ≥30 breaths/min | +20 | |
| Temperature <36°C | +20 | |
| Altered mental status | +60 | |
| Arterial oxyhemoglobin saturation level <90% | +20 | 1 |

[a] A total point score for a given patient is obtained by summing the patient's age in years and the points for each predictor when present. The score corresponds with the following risk classes: 65 or less, class I; 66 to 85, class II; 86 to 105, class III; 106 to 125, class IV; and more than 125, class V. Patients in risk classes I and II are defined as being at low risk.

[b] A total point score for a given patient is obtained by summing the points. The score corresponds with the following risk classes: 0, low risk; 1 or more, high risk. Empty cells indicate that the variable was not included.

[c] The variables were combined into a single category of chronic cardiopulmonary disease.

- Recurrences cluster in the first 2-3 months after discontinuation of anticoagulation, then decline reaching a plateau of:
  - <3% every year (provoked VTE)
  - 5-10% (unprovoked VTE)

- Prandoni et al: Risk after cessation of anticoagulation

| | |
|---|---|
| - 6 months | 8.6% |
| - 2 years | 17.5% |
| - 5 years | 24.8% |
| - 8 years | 30.3% |

# RISK ASSESSMENT FOR VTE RECURRENCE

NICE CG144

- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis. Continue for **3 months**. At 3 months consider risks and benefits of continuing VKA.
- Offer **LMWH** to patients with active cancer and confirmed proximal DVT or PE, and continue the LMWH for **6 months**. At 6 months, assess the risks and benefits of continuing anticoagulation.
- *Offer* a VKA **beyond 3 months** to patients with an **unprovoked PE**, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment.
- *Consider* extending the VKA **beyond 3 months** for patients with **unprovoked proximal DVT** if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment.

# RISK ASSESSMENT FOR VTE RECURRENCE

**ACCP recommendations, Chest, 2012**

| Patient categories | Drug | Duration (months) | Comments |
|---|---|---|---|
| First episode of DVT/ PE secondary to a transient (reversible) risk factor | VKA | 3 | Recommendation applies to both proximal and calf vein thrombosis |
| First episode of idiopathic DVT / PE | VKA | 6-12 | Continuation of anticoagulant therapy after 6–12 months may be considered |
| First episode of DVT/ PE and cancer | LMWH | 6 | Continuation of LMWH is recommended indefinitely or until the cancer is resolved |
| First episode of DVT/ PE with a documented thrombophilic abnormality | VKA | 6-12 | Continuation of anticoagulant therapy after 6–12 months may be considered |
| First episode of DVT/ PE with documented antiphospholipid antibodies or two or more thrombophilic abnormalities | VKA | 12 | Continuation of anticoagulant therapy after 12 months may be considered |
| Second episode of DVT/PE | VKA | | Consider indefinite duration anticoagulation |

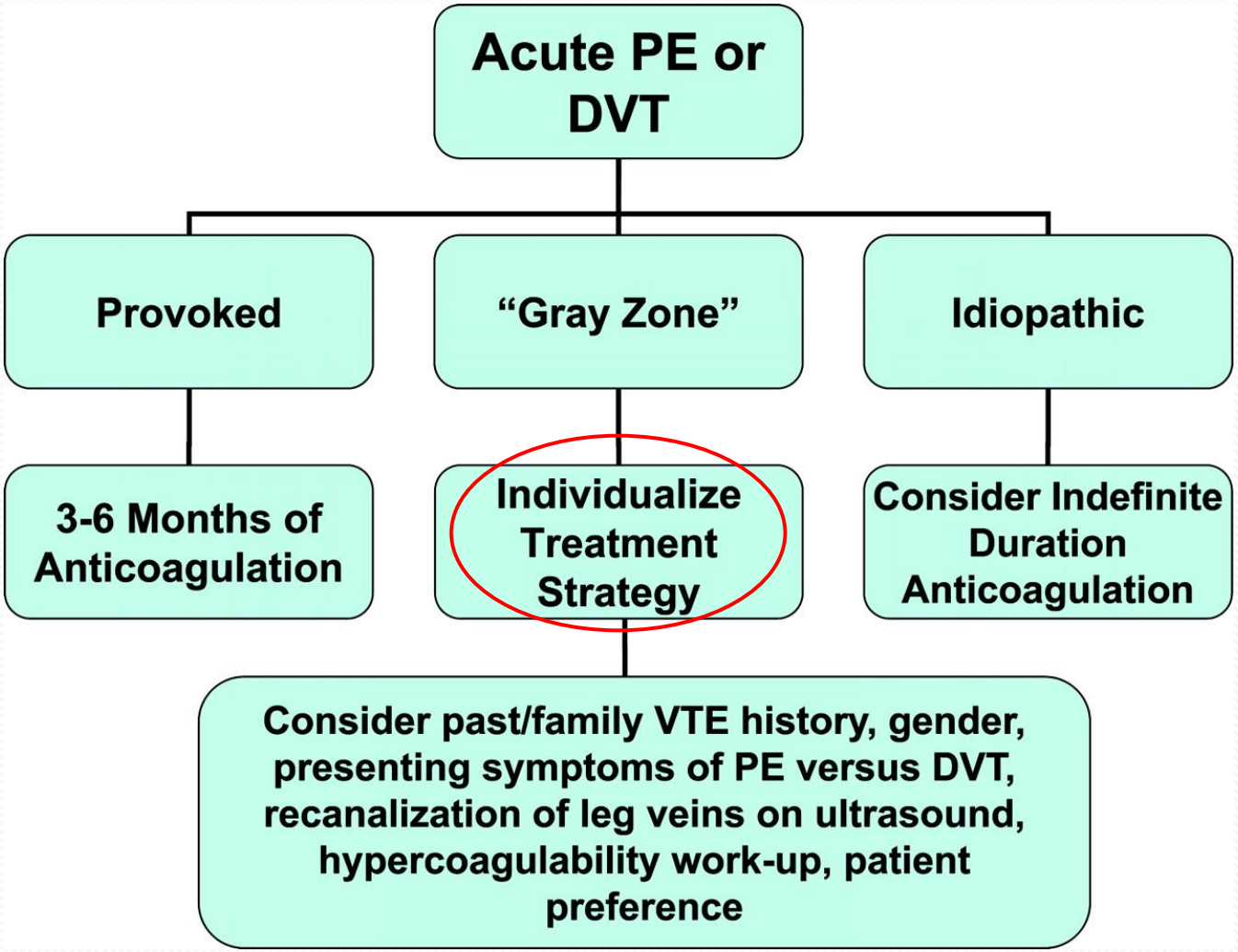
# RISK ASSESSMENT FOR VTE RECURRENCE

Factors NOT predictive of recurrence

- **VTE in pregnancy, OCP and gynae surgery**
- **Recent surgery, trauma or fracture.**
- **Recent immobilzation**
- **Hormonal therapy (Tamoxifen)**
- **Failed prophylaxis**
- **Distal DVT, deep muscular DVT**

***Short term oral anticoagulation 3/12 considered***

## Hybrid approach for optimizing the duration of anticoagulation in patients with VTE.




Goldhaber S Z , and Piazza G *Circulation*. 2011;123:664-667

# NOACs

- For more than 50 years VKAs were the only available anticoagulants
- September 2008- NICE TA157→ Dabigatran for primary VTE prevention (THR, TKR)
- TA170, TA1245 → Rivaroxaban, Apixaban for primary VTE prevention (THR, TKR)
- TA249, TA256, TA275 → Dabigatran,Rivaroxaban, Apixaban for prevention of stroke and systemic embolism in non valvular AF

- July 2012, TA261 → Rivaroxaban, DVT treatment, prevention of recurrent VTE and DVT
- June 2013, TA287 → Rivaroxaban, PE treatment, prevention of recurrent VTE

- Dabigatran for DVT, PE treatment and prevention (December 2014)
- Apixaban (June 2015)
- Edoxaban (October 2015)

# NOACs

**Comparison of the designs of the trials evaluating NOACs for extended VTE treatment**

| | **Dabigatran** | | **Rivaroxaban** | **Apixaban** |
|---|---|---|---|---|
| Trial | RE-SONATE | RE-MEDY | EINSTEIN-Ext | AMPLIFY-Ext |
| Comparator | Placebo | **Warfarin** | Placebo | Placebo |
| Design | Double-blind | Double-blind | Double-blind | Double-blind |
| Number of patients | 1343 | 2856 | 1197 | 2486 |
| Noninferiority margin | — | 2.85 | — | — |
| Duration of prior anticoagulation treatment (mo) | 6-18 | 3-12 | 6-12 | 3-12 |
| Treatment protocol | 150 mg BID | 150 mg BID | 20 mg OD | **2.5 or 5 mg BID** |
| Duration (mo) | 6 | 6-36 | 6-12 | 12 |

- All 3 superior to placebo for extended VTE treatment
- RE- MEDY - Dabigatran non inferior to warfarin
  - Less bleeding with dabigatran
  - MI more common with dabigatran

# NOACs

## Dosing information

### APIXABAN
**Dosing information**

5mg TWICE daily

Reduced dose:
2.5mg TWICE daily if…

- CrCl 15-29mL/min

Or two or more of:
- Age>80
- Weight<60kg
- SrCr >133mcmol/L

### DABIGATRAN
**Dosing information**

150mg TWICE daily

Reduced dose:
110mg TWICE daily if…
- Age > 80
- Concomitant VERAPAMIL

Consider 110mg over 150mg if:
- Age>75
- CrCl = 30–49mL/min
- GORD, gastritis
- HAS-BLED≥3

### RIVAROXABAN
**Dosing information**

20mg ONCE daily

Reduced dose:
15mg ONCE daily if…

- CrCl = 15–49mL/min
- HAS-BLED≥3

**The use of NOACs is NOT recommended if CrCl <15ml/min. Dabigatran contra-indicated if CrCl<30ml/min.**

**Check the current SmPC at www.medicines.org.uk for further information**

# Choosing the right anticoagulant for the right VTE patient

| Characteristic | Drug choice | Rationale |
|---|---|---|
| Extensive DVT or massive PE | Heparin | Such patients often require advanced therapy and were excluded from trials with the NOACs |
| High initial risk of bleeding | Heparin | Enables dose titration; rapid offset<br>Protamine as an antidote |
| Active cancer | LMWH | No trials comparing NOACs with LMWH |
| Pregnancy | LMWH | Warfarin and NOACs cross the placenta |
| Liver dysfunction with increased PT/INR at baseline | Warfarin | NOACs undergo hepatic metabolism |
| Limited access to anticoag clinic (impaired mobility or geographical inaccessibility) | NOAC | Given in fixed doses without monitoring |
| All-oral therapy | Rivaroxaban or apixaban | Only NOACs to be evaluated in all-oral regimens |
| Creatinine clearance <30 mL/min | Warfarin | Such patients were excluded from trials with NOACs |
| Creatinine clearance 30-50 mL/min | Rivaroxaban, apixaban, or edoxaban | Less affected by renal impairment than dabigatran; if edoxaban is chosen, the 30-mg OD dose should be used |
| Dyspepsia or upper gastrointestinal symptoms | Rivaroxaban, apixaban, or edoxaban | Dyspepsia in as much as 10% given dabigatran |
| Recent gastrointestinal bleed | Apixaban | More gastrointestinal bleeding with dabigatran, rivaroxaban, and edoxaban than with warfarin |
| Recent acute coronary syndrome | Rivaroxaban, apixaban or edoxaban | Small myocardial infarction signal with dabigatran |
| Poor compliance with long-term bd dosing | Rivaroxaban or edoxaban | OD regimens for long-term use |

# Special situations: Brain Metastases

- Brain tumours per se is not a contraindication to anticoagulation
- As to prophylaxis, benefits and risks have to be weighted individually using predictive scores such as the Khorana model
- In practice, we would give prophylactic treatment to patients with patients with high Khorana scores.

# NOACs

Potential limitations…

- Lack of specific antidotes APART FROM DABIGATRAN PRAXBIND as reversal available NICE approved 2016
- Adherence difficult to assess

# NOACs

Suggestions for further research…

- NOACs in cancer
- NOACs in patients with thrombophilia
- NOACs in HIT
- NOACs in patients requiring concomitant antiplatelet therapy
- NOACs in thrombocytopenic patients

# Case 1

- 73 yrs. old
- Admitted with SOB
- HB 34
- Blood test confirmed AIHA
- Transfused CT showed left axillary node
- Biopsy : AITL/CD20 positive
- Prednisolone started
- Readmitted with SOB and pulseless legs
- CT PA : confirmed PE on LMWH
- CT ANGIO: left legs Arterial clots

# Case 1 continued

- Had embolectomy

Failed

- Underwent above knee amputation
- Had milder chemotherapy Ritux and pred
- AW for RCHOP
- Admitted with pyrexia and SOB
- Blood test WCC 45
- 90% plasma cells : plasma cell leukaemia
- Palliative dexamethasone
- CT PA : massive bilateral PE expanding

# bloods

DLBCL, SOB, thrombocytopenia

**C REACTIVE PROTEIN**

Sample (TYPE UNKNOWN)Collected 06 Jun 2017 16:25 Received 06 Jun 2017 17:12

| | | | | |
|---|---|---|---|---|
| **C reactive protein** | * | 77 | mg/L | <5 |

**FULL BLOOD COUNT**

Sample (TYPE UNKNOWN)Collected 06 Jun 2017 16:25 Received 06 Jun 2017 17:12

| | | | | |
|---|---|---|---|---|
| **HAEMOGLOBIN** | * | 81 | g/L | 130 - 180 |
| **WHITE CELL COUNT** | * | 1.5 | $10^9$/L | 4.0 - 11.0 |
| **PLATELET COUNT** | * | 21 | $10^9$/L | 150 - 400 |
| **HCT** | * | 0.24 | L/L | 0.40 - 0.52 |
| **RCC** | * | 2.83 | $10^{12}$/L | 4.5 - 6.5 |
| **RDW** | * | 15.8 | % | 11.0 - 14.8 |
| **MCV** | | 85.7 | fL | 80 - 100 |
| **MCH** | | 28.8 | pg | 27.0 - 32.0 |
| **Differential Count** | | | | |
| **Neutrophil Count** | * | 0.24 | $10^9$/L | 1.7 - 7.5 |
| **Lymphocyte Count** | * | 0.43 | $10^9$/L | 1.5 - 4.5 |
| **Monocyte Count** | | 0.80 | $10^9$/L | 0.2 - 0.8 |
| **Eosinophils** | | 0.01 | $10^9$/L | 0.0 - 0.4 |

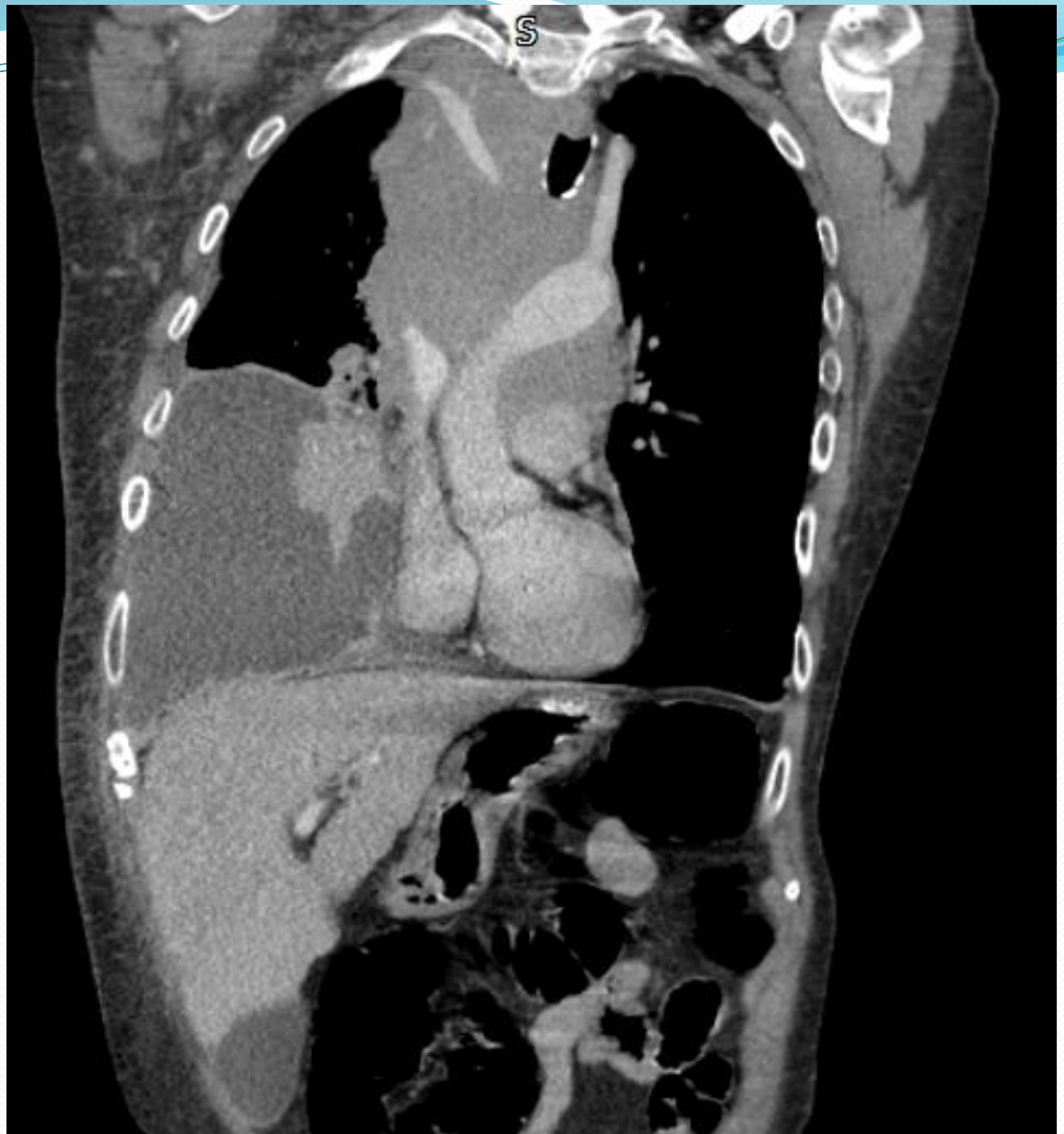
# Initial treatment of PE

- Transfuse platelets
- Keep PLT>50
- full dose LMWH
- Refractory thrombocytopenia needing daily transfusion
- DW/Carer and palliative care team
- Stop treatment and transfer to hospice
- RIP day 4

# Case 2
# 81 years old

- 6 weeks history of SOB
- Wt loss
- Night sweat
- Left leg swelling
- Previously
- IVDU and on Methadone replacement
- HEP C positive for watch and wait

# CT



# Emergency

- Chest drain
- Pleural fluid flow: Confirmed DLBCL
- BMAT: Consistent DLBCL
- Urgent; Dexamethasone 40 mg
- Emergency RT for SVC obstructions
- Had Rituxmab and Prednisolone
- Stable and escalate to RCHOP X6
- Was in CR
- Had IT MTX X4

# Readmitted with Pleuritic chest pain and fits

- CT PA : PE
- MRI: brain lymphoma
- Dex started and initiated RT to brain as palliative approach
- Deteriorated with sepsis and further fits
- Stopped all medication
- RIP as inpatient day 8

# Case 3
# 55 years old

- AML
- Treated with intensive chemo
- Had allo SCT
- Severe GVHD
- On long term immunosuppressive
- Admitted with legs cellulitis
- Spread rapidly and became Necrotising fasciitis
- Emergency debridement
- HL : blocked
- US: extensive clots

Sample [redacted]-4(TYPE UNKNOWN)Collected 18 Jun 2017 08:55 Received 18 Jun 2017 09:48

| | | | | |
|---|---|---|---|---|
| **HAEMOGLOBIN** | * | 107 | g/L | 115 - 165 |
| **WHITE CELL COUNT** | | 8.6 | $10^9$/L | 4.0 - 11.0 |
| **PLATELET COUNT** | * | 43 | $10^9$/L | 150 - 400 |
| **HCT** | * | 0.33 | L/L | 0.37 - 0.46 |
| **RCC** | * | 2.80 | $10^{12}$/L | 3.8 - 5.8 |
| **RDW** | * | 21.7 | % | 11.0 - 14.8 |
| **MCV** | * | 117.1 | fL | 80 - 100 |
| **MCH** | * | 38.1 | pg | 27.0 - 32.0 |
| **Differential Count** | | | | |
| **Neutrophil Count** | | 7.08 | $10^9$/L | 1.7 - 7.5 |
| **Lymphocyte Count** | * | 0.83 | $10^9$/L | 1.5 - 4.5 |
| **Monocyte Count** | | 0.66 | $10^9$/L | 0.2 - 0.8 |
| **Eosinophils** | | 0.02 | $10^9$/L | 0.0 - 0.4 |
| **Basophils** | | 0.01 | $10^9$/L | 0.0 - 0.1 |

**SERUM FERRITIN**

Sample [redacted]PE UNKNOWN)Collected 18 Jun 2017 08:55 Received 18 Jun 2017 09:48

| | | | | |
|---|---|---|---|---|
| **Serum Ferritin** | * | 2135 | ng/ml | 15 - 300 |

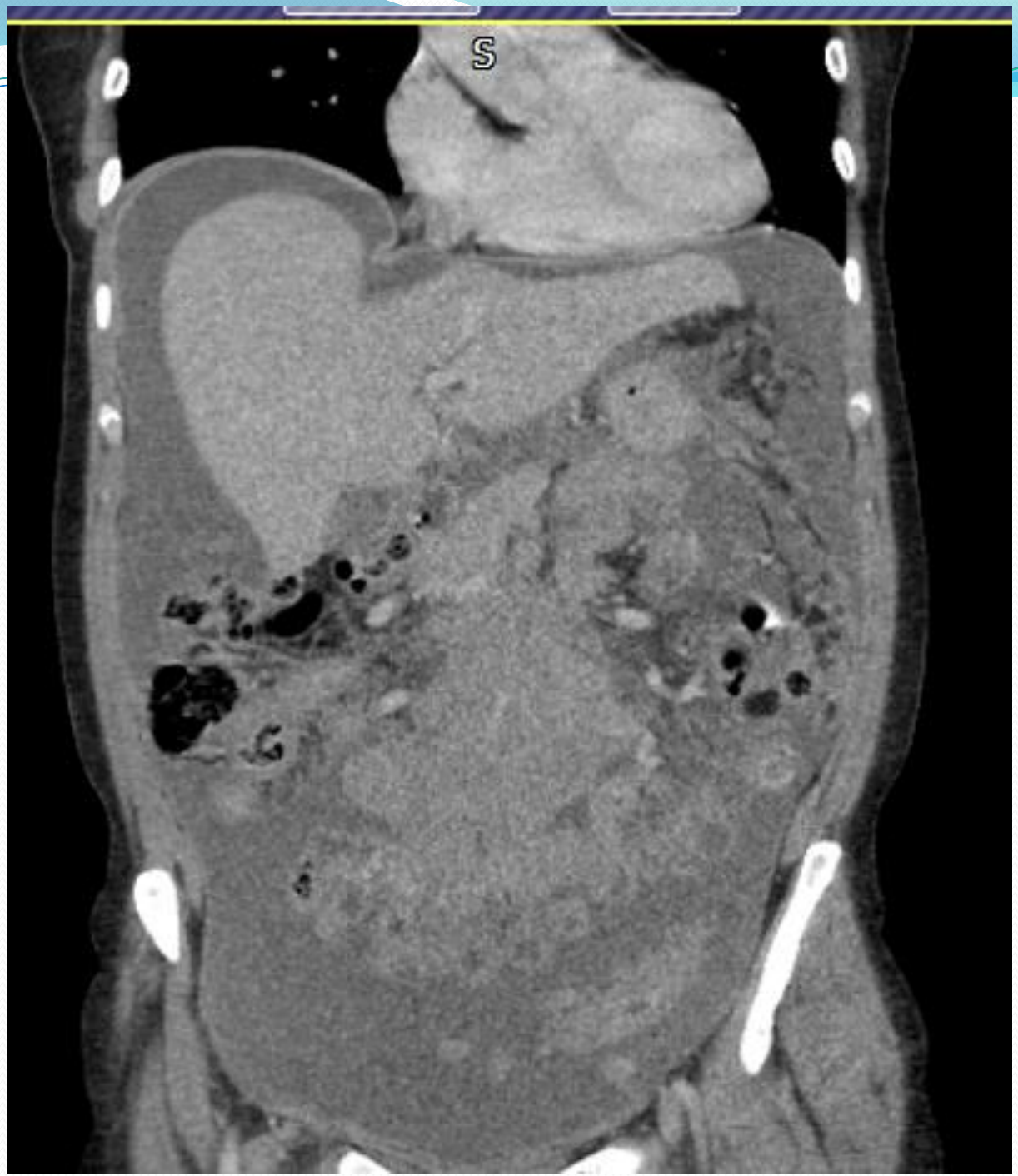
Elevated ferritin; iron has been added to this request.

- Had intermediate dose LMWH
- Plan for HL removal Day 3 then line removal
- Patient deteriorated day 15 and RIP

# Case 4
# 57 yrs. old

- Abdominal pain and distension for 6 weeks
- Non specific B symptoms
- Left leg swealling
- Bloods: normal
- Reviewed in OG opd and admitted
- Had US and CT
- Us doppler : extensive DVT
- LMWH started

# CT



# O&G admission

- For complex abdominal open surgery
- Haematology advise
- Stop LMWH and insert IVC filter
- TEDs stocking
- Monitoring
- Day 10 post surgery: biopsy DLBCL for CHEMO
- Removal of IVC filter and LMWH started

# Case 5

# 56 yrs. old lady

- Metastatic ovarian cancer
- Left leg DVT and PE
- Bloods Stable: PLT 600
- Clotting Normal
- LMWH started as treatment dose
- Patient find SC too painful and extensive abdominal wall bruising
- What to give ?
- Opted for Dabigatran
- We have reversal in case of bleeding
- Patient was transgffered to Hospice and died 5 weeks after transfer

# Case 6
# 60 yrs. old known T cell lymphoma

- CHOEP chemotherapy X6 - PR
- ASCT and PD
- Failed Brentuximab
- SOB
- CT PA: Bilateral PE

?sepsis - known relapsed angioimmunoblastic T cell lymphoma after autologous ste

**C REACTIVE PROTEIN**

Sample [redacted]TYPE UNKNOWN)Collected 21 Nov 2016 12:00 Received 21 Nov 2016 12:22

| | | | | |
|---|---|---|---|---|
| **C reactive protein** | * | 67 | mg/L | <5 |

**FULL BLOOD COUNT**

Sample [redacted]?(TYPE UNKNOWN)Collected 21 Nov 2016 12:00 Received 21 Nov 2016 12:22

| | | | | |
|---|---|---|---|---|
| **HAEMOGLOBIN** | * | 90 | g/L | 130 - 180 |
| **WHITE CELL COUNT** | * | 1.8 | $10^9$/L | 4.0 - 11.0 |
| **PLATELET COUNT** | * | 39 | $10^9$/L | 150 - 400 |
| **HCT** | * | 0.28 | L/L | 0.40 - 0.52 |

Please note change in FBC method from 27/09/16.
No significant differences in results expected.

| | | | | |
|---|---|---|---|---|
| **RCC** | * | 2.91 | $10^{12}$/L | 4.5 - 6.5 |
| **RDW** | * | 20.5 | % | 11.0 - 14.8 |
| **MCV** | | 96.7 | fL | 80 - 100 |
| **MCH** | | 31.0 | pg | 27.0 - 32.0 |
| **Differential Count** | | | | |
| **Neutrophil Count** | * | 1.31 | $10^9$/L | 1.7 - 7.5 |
| **Lymphocyte Count** | * | 0.40 | $10^9$/L | 1.5 - 4.5 |
| **Monocyte Count** | * | 0.08 | $10^9$/L | 0.2 - 0.8 |
| **Eosinophils** | | 0.00 | $10^9$/L | 0.0 - 0.4 |
| **Basophils** | | 0.02 | $10^9$/L | 0.0 - 0.1 |

**FULL CLOTTING SCREEN**

| | | | | |
|---|---|---|---|---|
| **Basophils** | | 0.07 | $10^9$/L | 0.0 - 0.1 |
| **PHOSPHATE** | | | | |
| Sample (TYPE UNKNOWN) Collected 05 Jul 2017 12:40 Received 05 Jul 2017 15:38 | | | | |
| **Phosphate** | | 1.37 | mmol/L | 0.8 - 1.5 |
| **TRANSFERRIN** | | | | |
| Sample (TYPE UNKNOWN) Collected 05 Jul 2017 12:40 Received 05 Jul 2017 15:38 | | | | |
| **Transferrin** | * | 1.6 | g/L | 2.0 - 3.6 |
| **Iron** | | 10.8 | umol/L | 10 - 30 |
| **Transferrin %saturation** | | 27 | % | 15 - 45 |
| **UREA & ELECTROLYTES** | | | | |
| Sample (TYPE UNKNOWN) Collected 05 Jul 2017 12:40 Received 05 Jul 2017 15:38 | | | | |
| **Sodium** | | 136 | mmol/L | 133 - 146 |
| **Potassium** | * | 6.5 | mmol/L | 3.5 - 5.3 |
| **Urea** | * | 21.7 | mmol/L | 2.5 - 7.8 |
| **Creatinine** | * | 710 | umol/L | 45 - 104 |

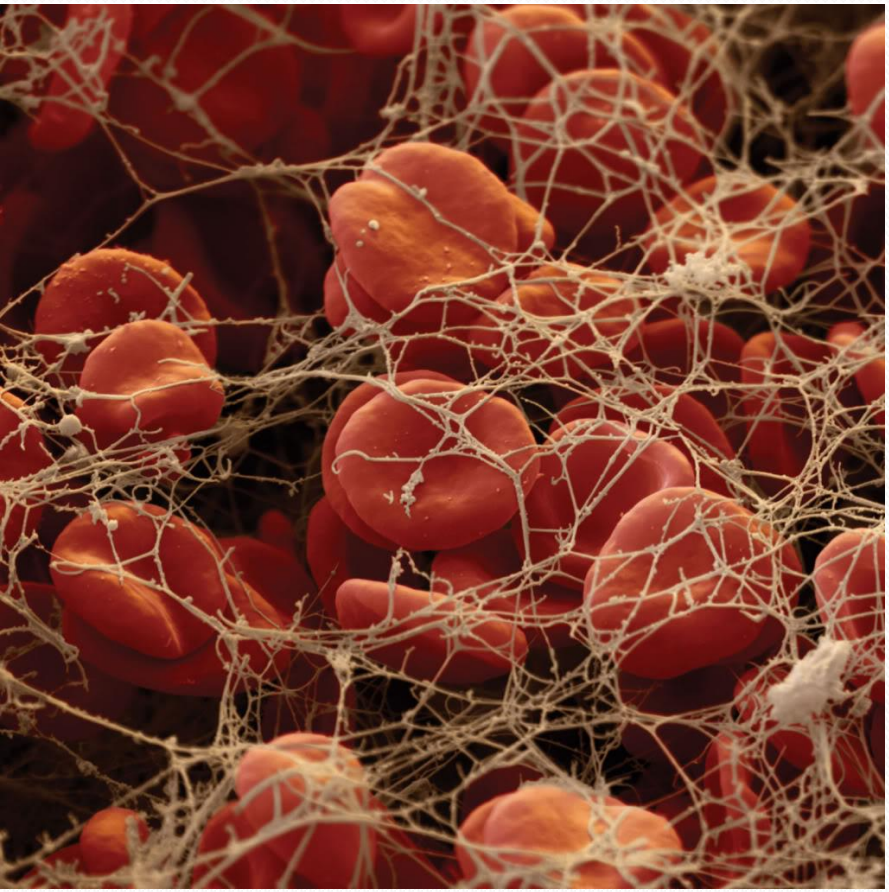
# IV heparin started

- patient deteriorated
- RIP day 5

# Few more points

- Prophylaxis with LMWH if PLT>30 and normal renal function and clotting
- Careful monitoring essential
- Risk benefit must be discussed with patient/relatives and careers
- NOACs not licensed but should be consider on case by case basis

- If needed then DABIGATRAN preferred as we have now reversal: Praxbind
- IVC filter is temporary >3 months at best if palliative and prognosis is poor any way then leave in situ
- In emergency and multiorgan failure with VTE: IV heparin preferable



Thank you !