VTED in HIV

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Venous Thromboembolism comprises the continuum of DVT to pulmonary thromboembolism.

DVT is the precursor of pulmonary emboli, therefore the risk factors for DVT are the same for pulmonary embolus and the treatment is essentially similar, however patients with an initial PE have a higher 1 month mortality and are 3 times more likely to have a recurrent PE than patients presenting with an isolated DVT.

Epidemiology

- Estimated incidence rate of 1/1000 person years in the general population
- Occurrence of VTE in HIV-infected persons 0.19-7.3%/year (2-10 fold higher risk)
- Pregnancy: Annual incidence in HIV infected women during puerperium 313/1000 person years (157 fold higher compared to HIV negative pregnant women, 120 fold higher than HIV infected controls)

FREQUENCY

40
35
30
25
20
15
10
5
0

Deep venous thrombosis
Hypertension
Pulmonary tuberculosis
HIV infection
Diabetes mellitus
Cigarette smoking
Pueperium
Dilated cardiomyopathy
Obesity
Acute myocardial infarctio
Alcohol
Fracture long bone
Stroke
Pneumonia
Malignancy

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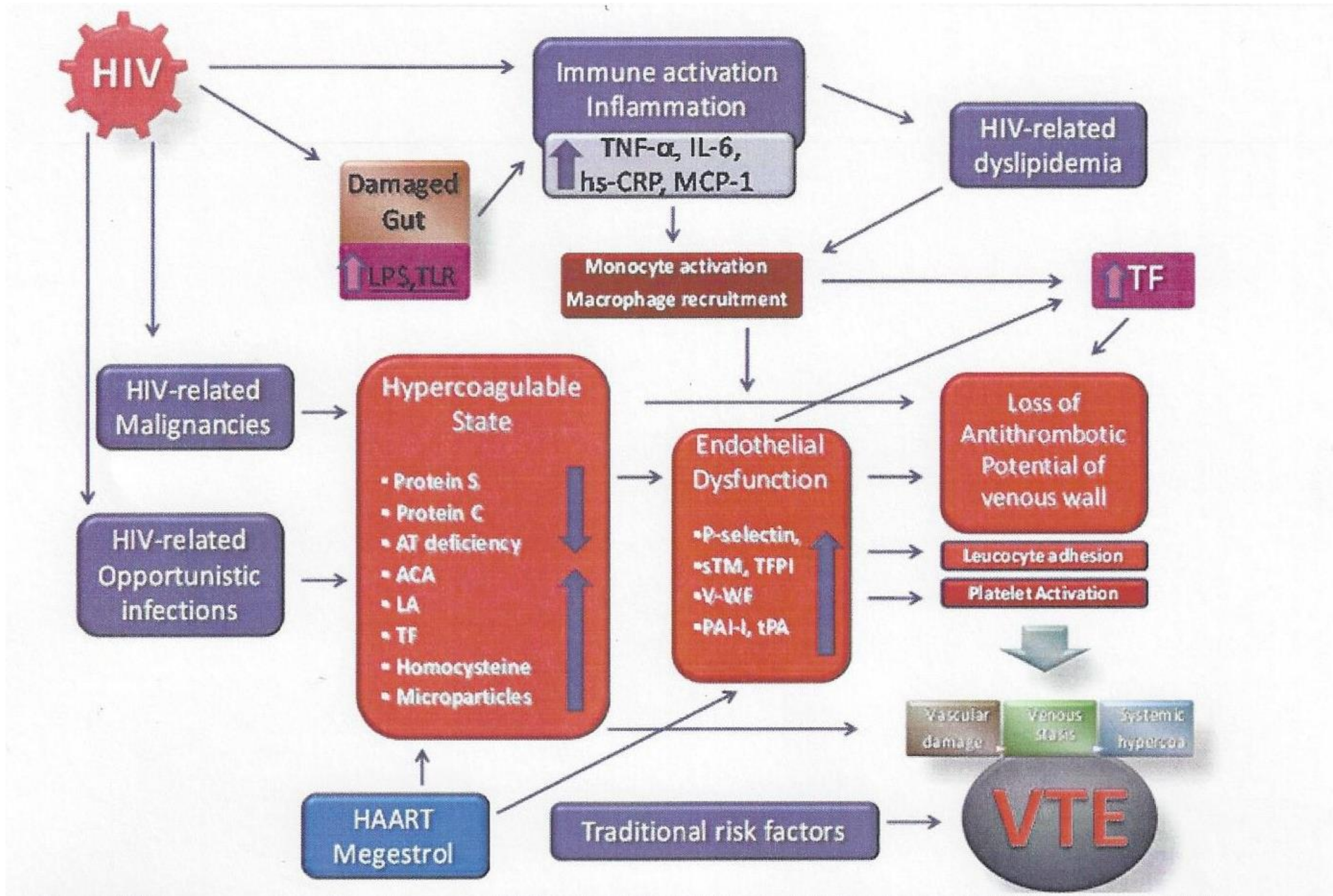

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GENETIC RISK FACTORS:
- AT Deficiency
- Protein C Deficiency
- Protein S Deficiency
- Factor V Leiden
- Factor II G20210A

VIRAL RISK FACTORS:
- CD4+ < 200
- Detectable Viral Load

ACQUIRED TRADITIONAL RISK FACTORS:
- Advancing Age
- Obesity (BMI >30)
- Previous Thrombosis
- Cigarette Smoking
- Hypertension
- Immobilization
- Injecting Drug Use
- Pregnancy

HIV-RELATED HYPERCOAGULABLE STATE:
- Protein S deficiency
- Protein C deficiency
- AT deficiency
- Antiphospholipid syndrome
- Tissue factor
- Homocysteine
- Microparticles

HIV & VTE

OPPORTUNISTIC INFECTIONS :
- Cytomegalovirus
- Tuberculosis
- Pneumocystis jiorveci

ENDOTHELIAL DYSFUNCTIONS:
- P-selectin
- sTM, TFPI
- v-WF
- PAI-I, tPA

HIV-RELATED MALIGNANCIES:
- Kaposi Sarcoma
- Non-Hodgkin Lymphoma
- Solid Tumors

IATROGENIC:
- Indwelling catheters
- Surgery
- Protease inhibitors
- Megestrol Acetate
- Rifampicin

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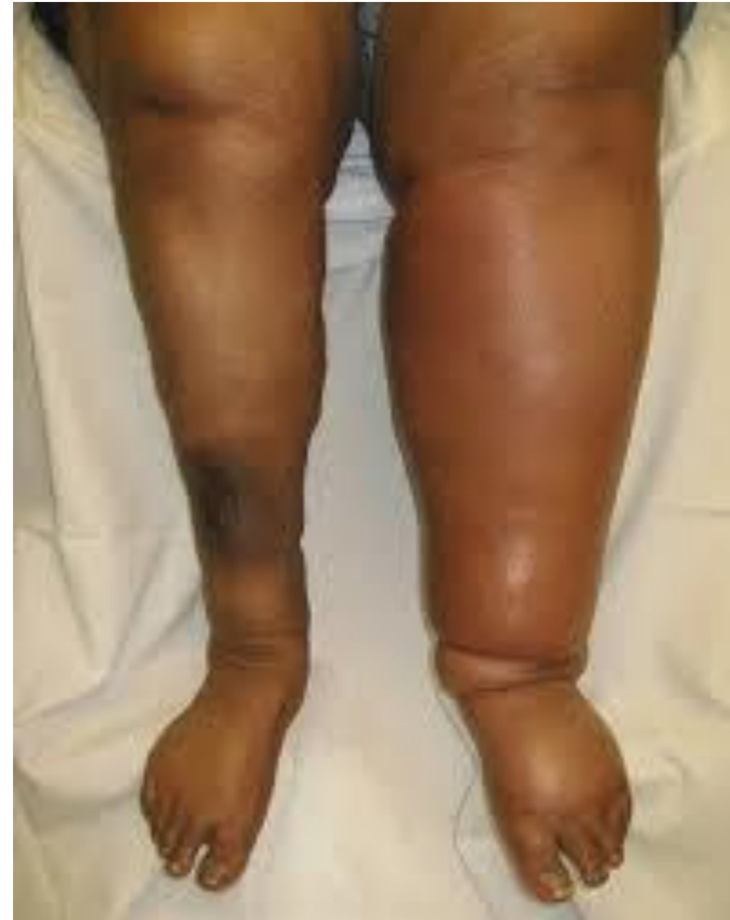
Diagnosis

- Symptoms in HIV are the same.
- In large series < 30% with typical symptoms had confirmed DVT.
- HIV infected patients may have symptoms related to other HIV associated conditions such as neuropathy, hypoproteinaemia and respiratory infections



Clinical Decision Rules

- Unknown generalizability to HIV infected population
- D- dimers raised in 40-60% of hospitalized medical patients. May be raised in HIV infection

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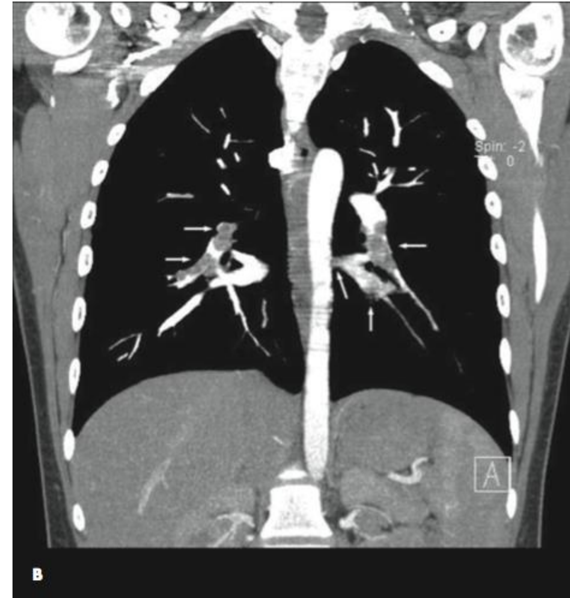
Variable	Points
Clinical signs and symptoms of DVT*	3.0
An alternative diagnosis is less likely than PE	3.0
Heart rate >100 beats per minute	1.5
Immobilization or surgery in previous 4 weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the last 6 mos or palliative)	1.0

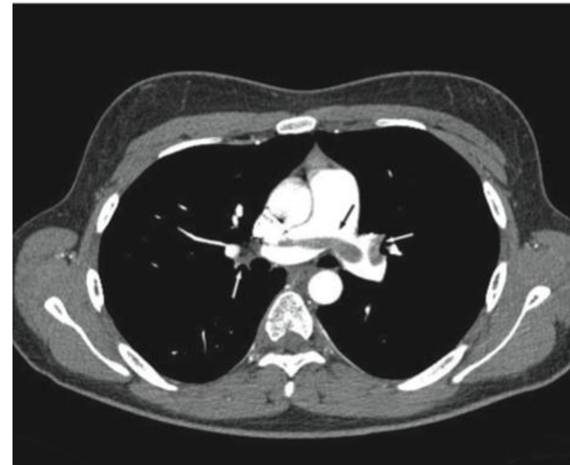
**Minimum of leg swelling and pain with palpation of deep veins; DVT, deep-vein thrombosis; PE, pulmonary embolism*

Score	Category	Score	Category
<2 points	low probability	<4 points	unlikely PE
2–6 points	moderate probability	≥4 points	likely PE
>6 points	high probability		

Source: Lab Med © 2008 American Society for Clinical Pathology

Diagnostic imaging





Treatment

- Isolated Distal DVT: Serial imaging for 2/52
  Or anticoagulation for 3/12
- Proximal DVT or PE with temporary risk factor :anticoagulation for 3/13
- Unprovoked DVT or PE: anticoagulation for 3/12 consider extending duration in patients at low to moderate risk for bleeding
- Consider extension beyond 3/12 HERDOO2

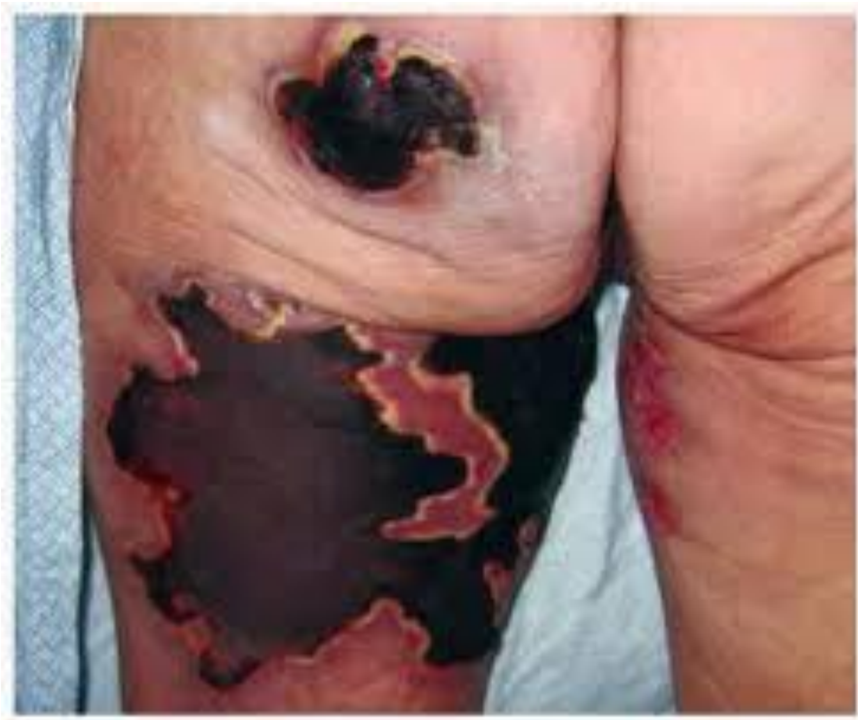
Choice of anticoagulant

- Initial parenteral, SC LMWH (or IV UFH if renal dysfunction)
- Oral Vitamin K antagonist started early (same day)
- Continue parenteral anticoagulation for a minimum of 5 days and INR >2 for at least 24hrs

Problems with VKA

- Individual variation
- Drug interactions: Rifampicin, Protease Inhibitors, NNRTIs
- Case series of HIV infected persons on oral VKA in an urban primary care setting found 71.6% of INR measurements were outside the therapeutic range with 51.5% being below and 21.2% above the range. INRANGE study 40.4% of INRs out of range.

Later's
WARFARIN
BAIT
KILLS NORWAY (SEWER) RATS, ROOF RATS & MICE
EFFECTIVE CONTROL FOR RATS AND MICE
IN AND AROUND THE HOUSE
500 g



4.0

RHI

Direct Oral Anticoagulants

- Dabigatran (Pradaxa): direct thrombin inhibitor. Absorption mediated by P-glycoprotein. Avoid with P-gp inhibitors : Protease Inhibitors and P-gp inducers : rifampicin and tenofovir

- Rivaroxaban (Xerelto) direct factor Xa inhibitor. Absorption mediated by P-glycoprotein. Metabolism mediated by CYP3A4.
- Avoid with: Protease inhibitors, rifampicin, rifabutin, efavirenz, neveripine, etravirine
- DOACs: no routine therapeutic monitoring available. Not reversible.

Summary

- HIV infection is prothrombotic and prevention is essential.
- VTE common in HIV, especially low CD4 cell count, hospitalization and Oi’s such as TB and PCP and prophylaxis should be used
- Traditional Clinical Decision rules are not appropriate
- Therapy is difficult and duration should be individualized