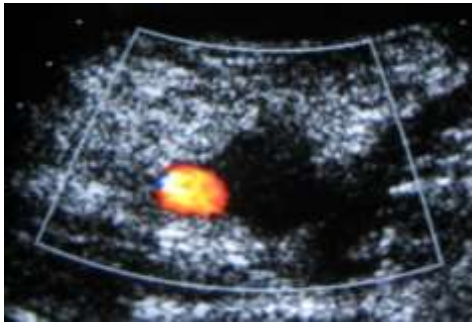
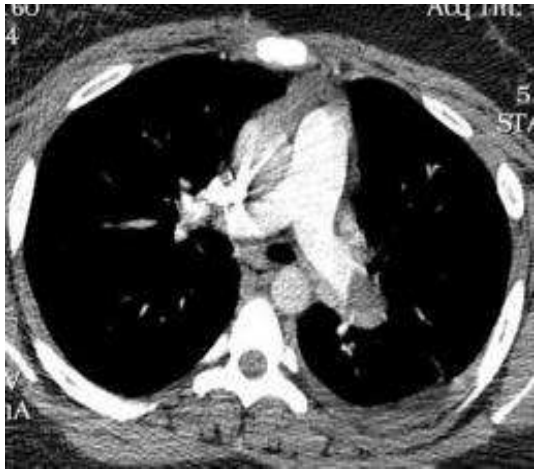
Case 7:

49 yr old lady complains of painful swelling and hotness of her L leg following coming back from visiting her relatives in USA. She had repeated attacks of cough with hemoptysis and shortness of breath. P/E

Duplex Us: DVT common femoral vein with

PE

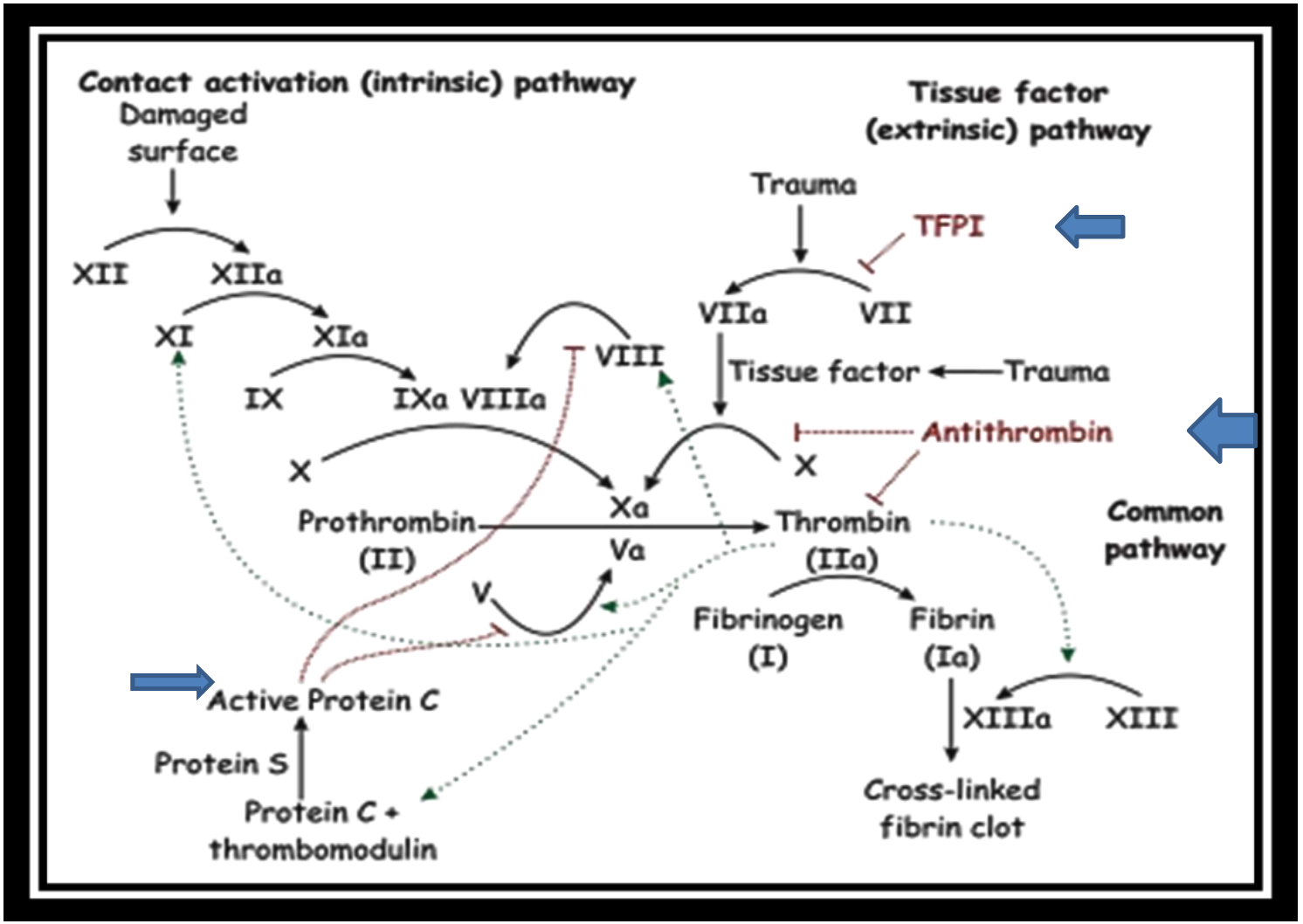




DVT



Case 10 investigation & Diagnosis



Importance of VTE (DVT/PE)

A- PREVENTABLE

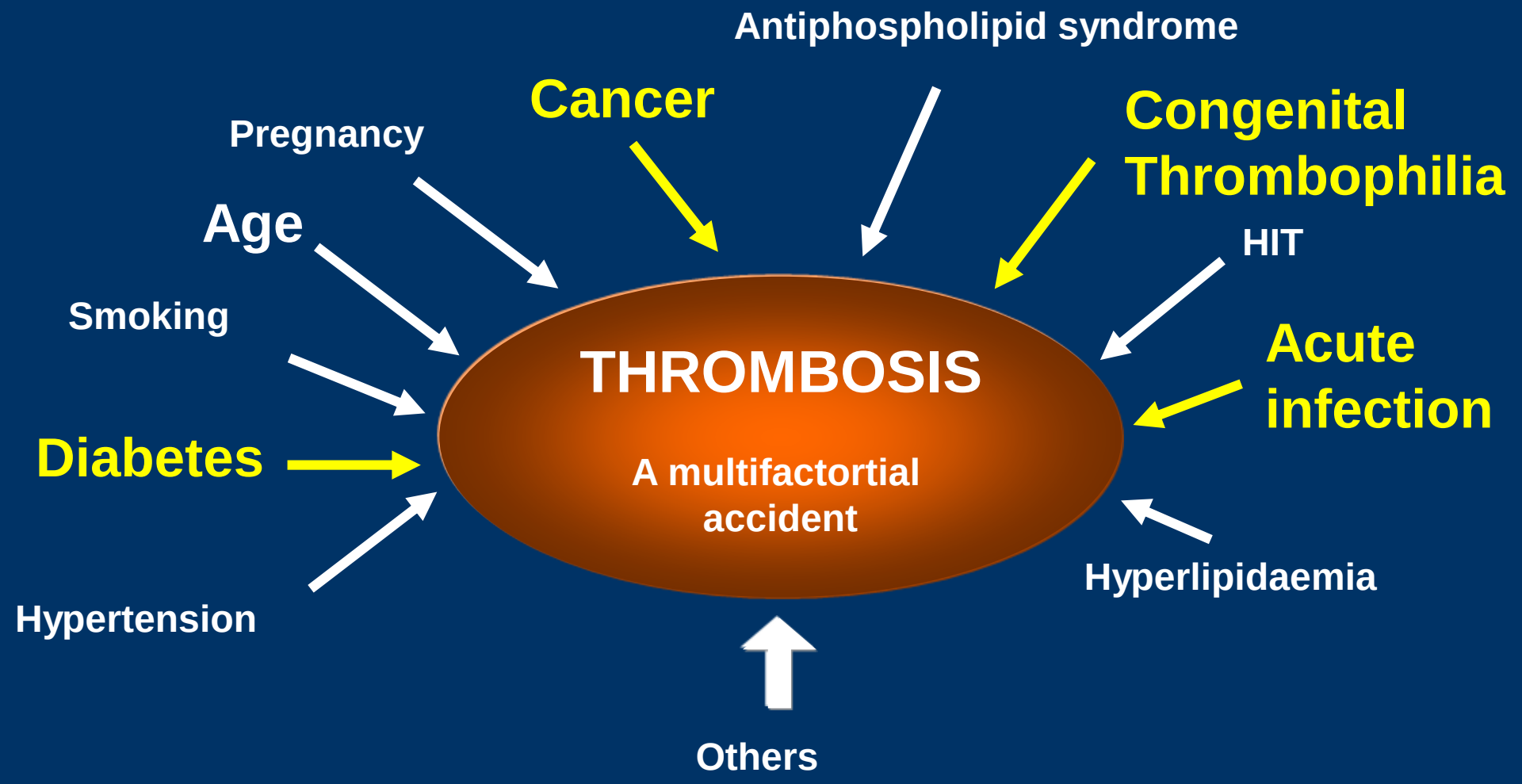
B- LIFE THREATENING

C- LONG TERM COMPLICATIONS

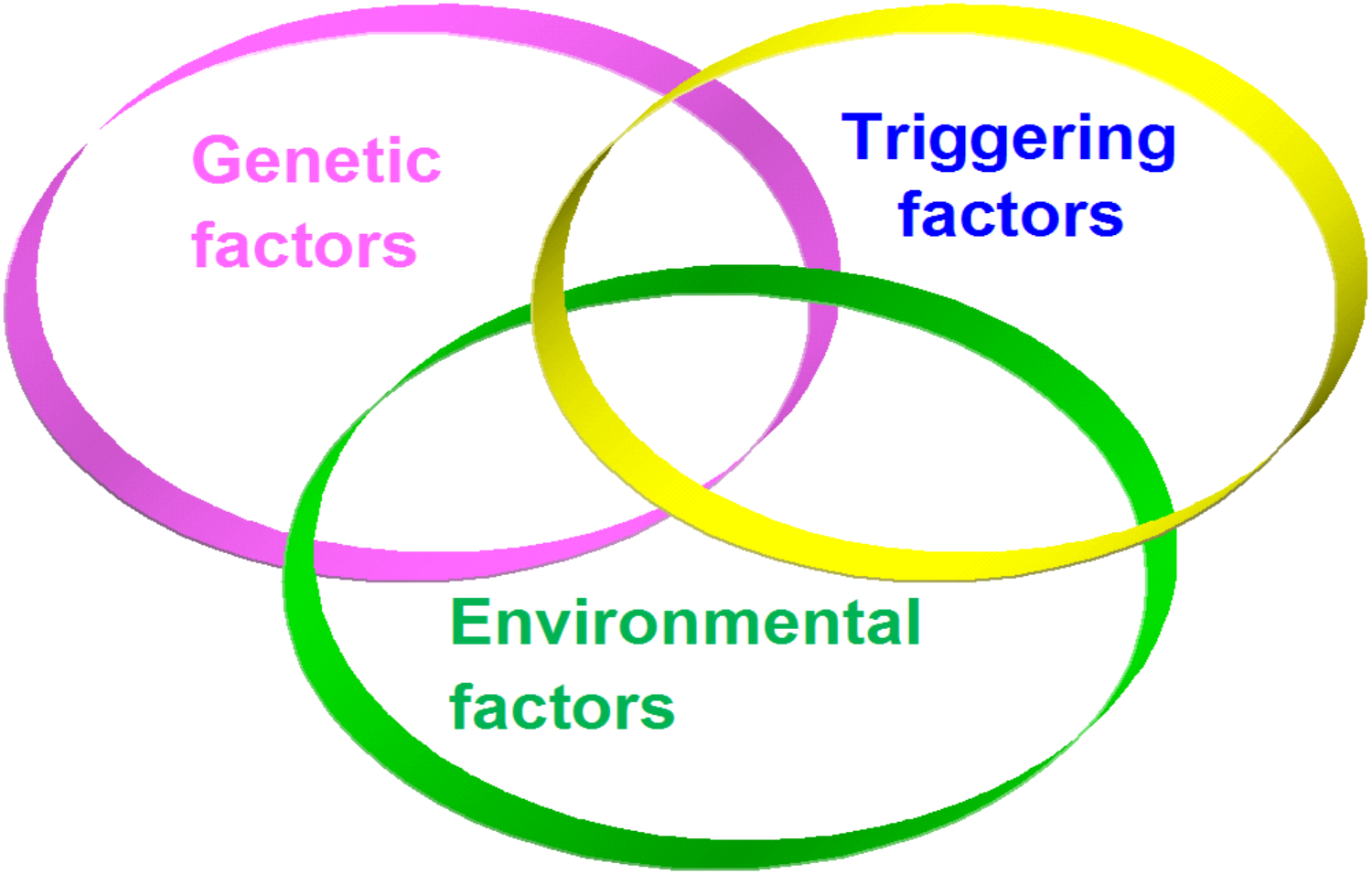
D- COMMON

E- COSTLY

VTE is a multifactorial and often silent disease



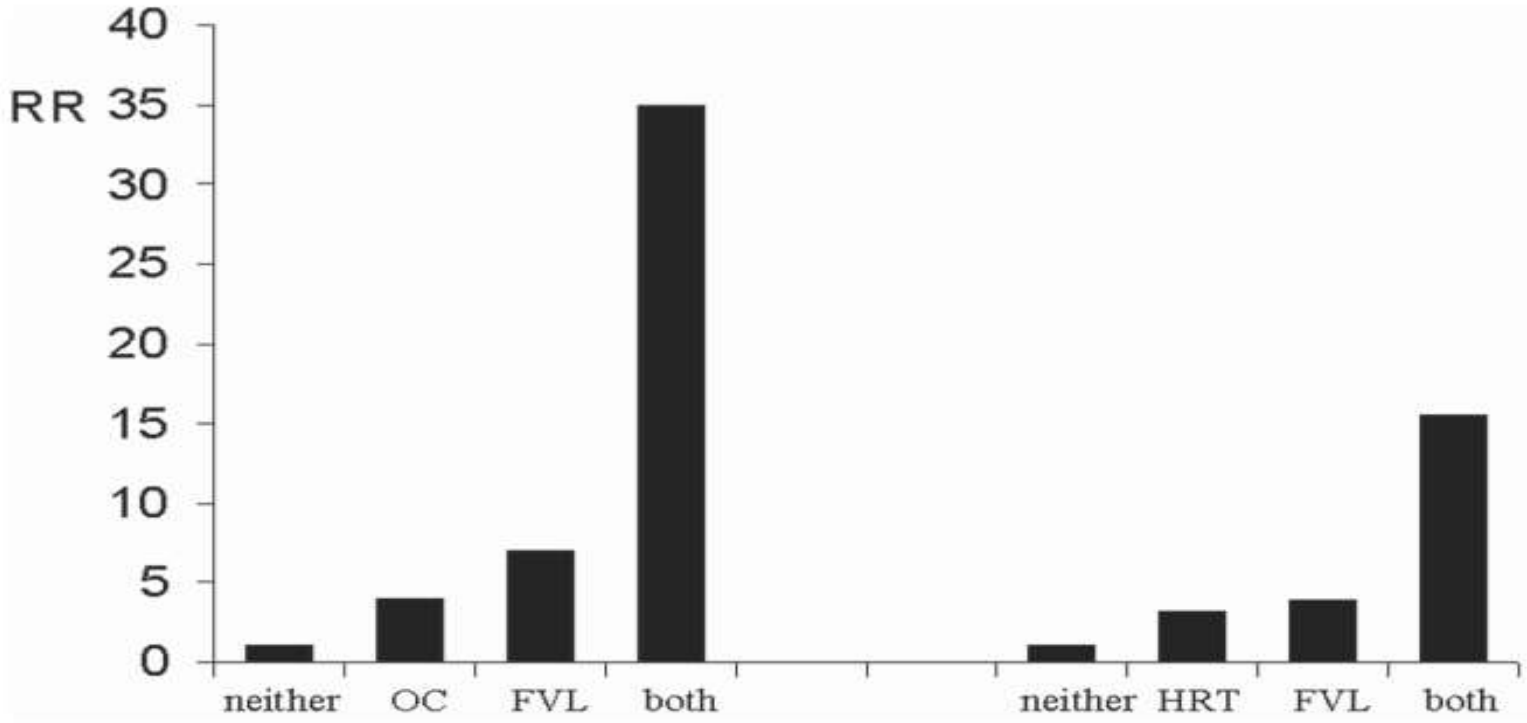
Venous thrombo-embolism is a multifactorial disease



Important Genetic Factors

1- Protein C defeiciency
2- Protein S deficiency
3- ATIII deficiency
4- Factor V Leiden mutation
5- Prothrombin (factor II) mutation

Combined risk factors (inherited + acquired) are key to high risk for VTE



Absolute risk 1 per 16,000/yr healthy premenopausal women

Figure 1. Interaction of factor V Leiden and oral contraceptive use (left panel),[89] and factor V Leiden and hormonal replacement therapy (right panel).[90]

Risk Factors for VTE

Stasis

- Age > 40
- Immobility
- CHF
- Stroke
- Paralysis
- Spinal Cord injury
- Hyperviscosity
- Polycythemia
- Severe COPD
- Anesthesia
- Obesity
- Varicose Veins

Hypercoagulability

- Cancer
- High estrogen states
- Inflammatory Bowel
- Nephrotic Syndrome
- Sepsis
- Smoking
- Pregnancy
- Thrombophilia

Endothelial Damage

- Surgery
- Prior VTE
- Central lines
- Trauma

Anderson FA Jr. & Wheeler HB. *Clin Chest Med* 1995;16:235.

Risk Factors for VTE

Stasis

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Hypercoagu

- Cancer
- High
- I
- me
- g
- egnancy
- Thrombophilia

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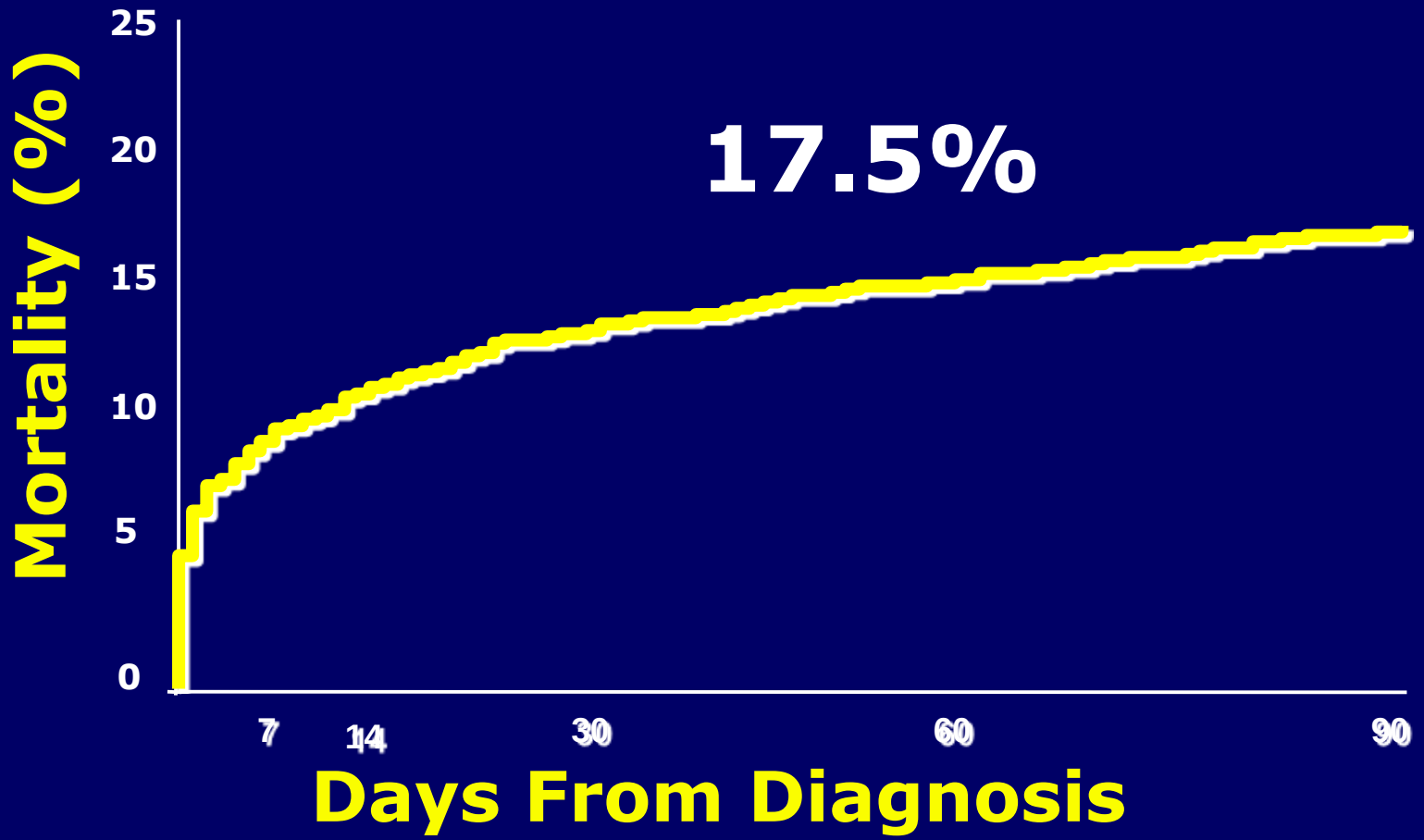
- Surgery
- Prior VTE
- Central lines
- Trauma

Most hospitalized patients have at least one risk factor for VTE

Anderson FA Jr. & Wheeler HB. *Clin Chest Med* 1995;16:235.
Bick RL & Kaplan H. *Med Clin North Am* 1998;82:409.

ICOPER: Cumulative Mortality after Diagnosis



Lancet. 1999;353:1386-1389.

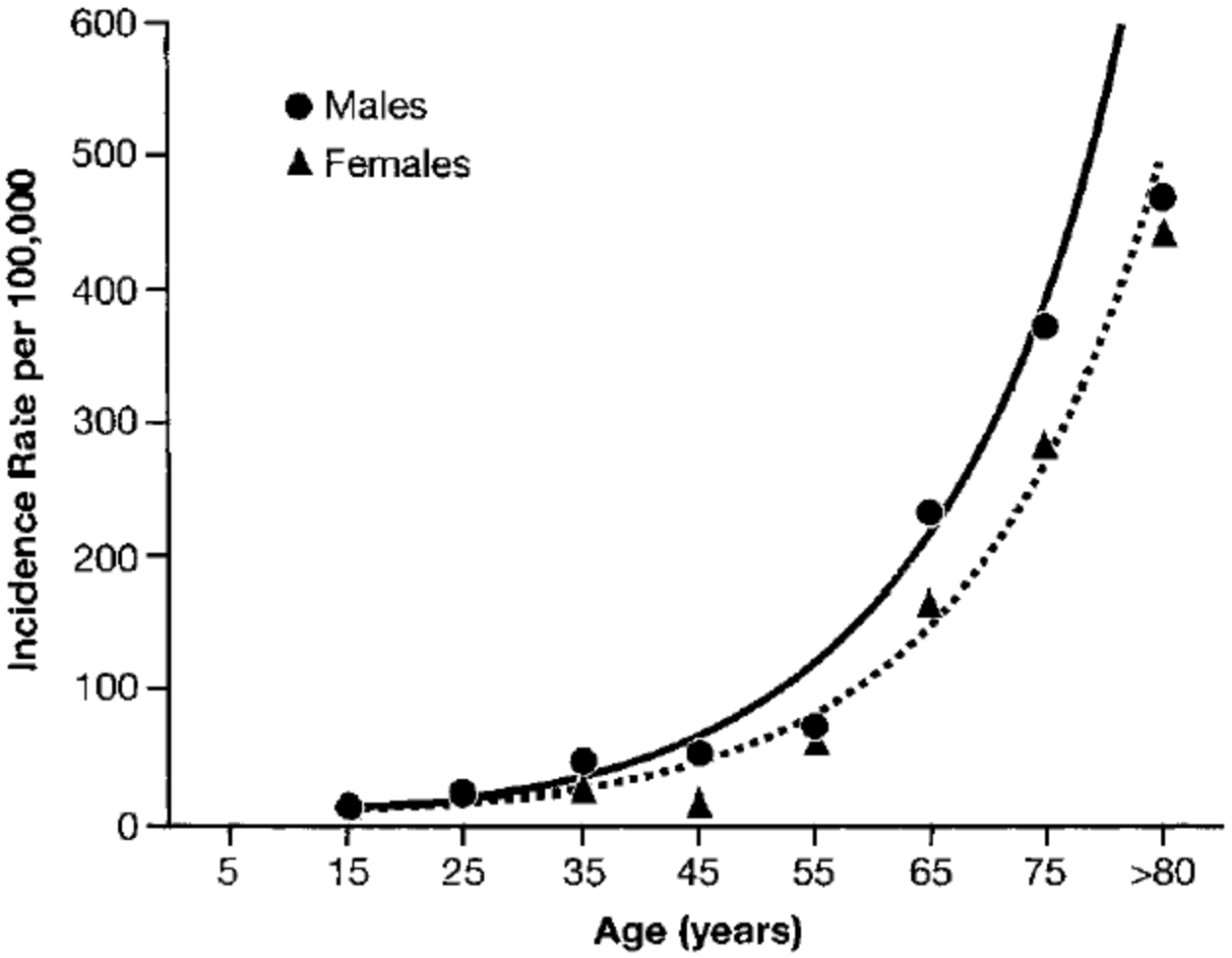
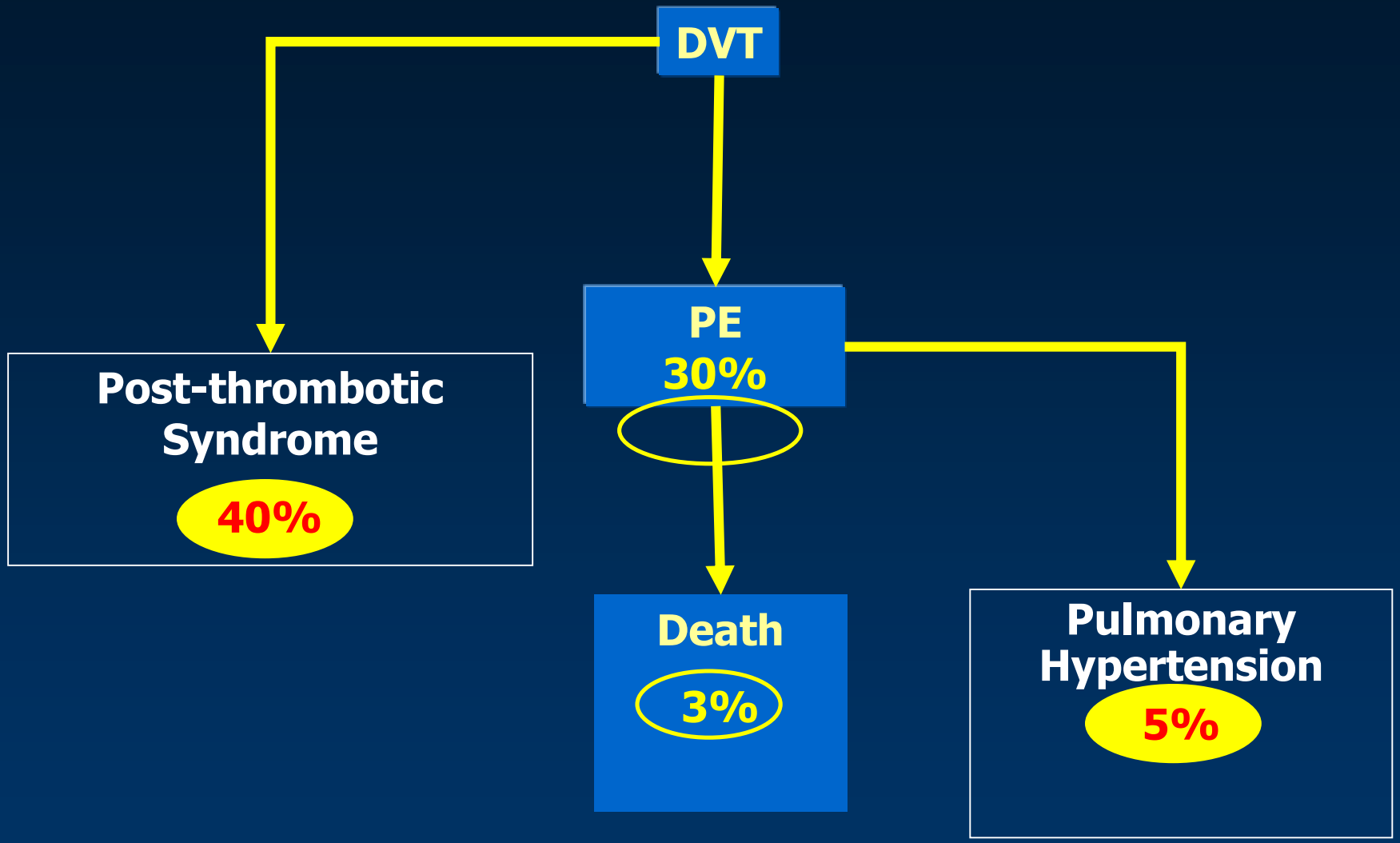


Figure 1. Annual incidence of VTE among residents of Worcester MA 1986, by age and sex. (Reproduced by permission from Anderson FA, et al. *Arch Intern Med*. 1991;151:933–938.)

The Burden of Venous Thrombo Embolism

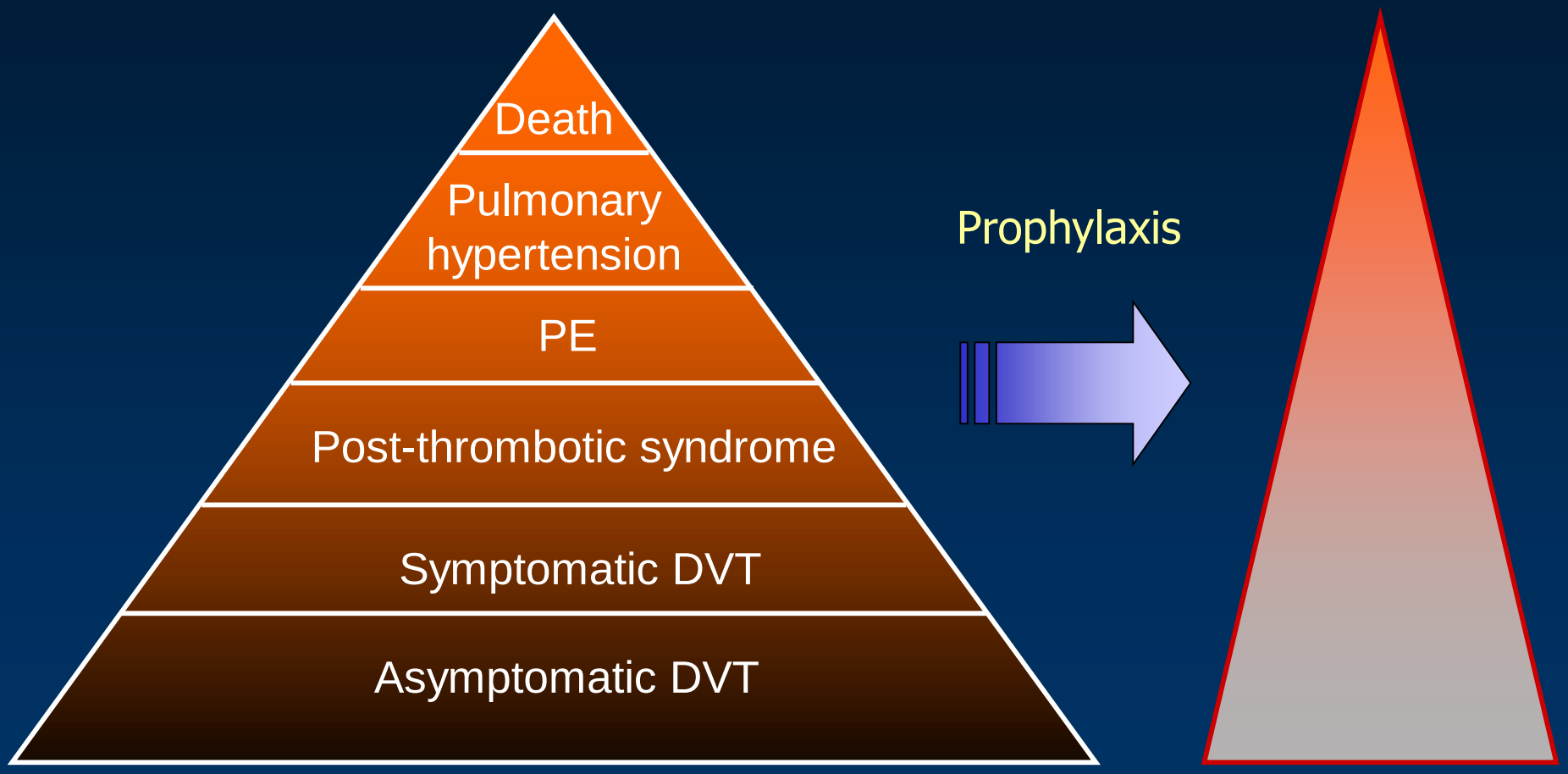


[1]Brandjes DP et al. Lancet 1997;349:759-62
[2]Kahn SR et al. Arch Intern Med. 2004 Jan 12;164(1):17-26.
[3]Hirsh J & Hoak J. Circulation 1996;93:2212-45
[4]Peng et al. NEJM 2004;350:2257-64

Post DVT Syndrome/ V.Stasis



Thromboprophylaxis reduces the burden of VTE



Hirsh J, Hoak J. Circulation. 1996;93:2212-45.

Risk Assessment for VTE

Identifying at-risk patient

↓

Counselling at-risk patient

↓

Prescribing thromboprophylaxis

Jordan University Hospital

Venous Thromboembolism Risk Factor Assessment

Patient's Name:_____ Age: ____ Sex: ____ Wgt:____Kg.

Hospital No. _____

Choose All That Apply

Each Risk Factor Represents 1 Point

- ☐ Age 41-60 years
- ☐ Minor surgery planned
- ☐ History of prior major surgery
- ☐ Varicose veins
- ☐ History of inflammatory bowel disease
- ☐ Swollen legs (current)
- ☐ Obesity (BMI >30)
- ☐ Acute myocardial infarction (< I month)
- ☐ Congestive heart failure (< 1 month)
- ☐ Sepsis (< 1 month)
- ☐ Serious lung disease incl. pneumonia (< 1 month)
- ☐ Abnormal pulmonary function (COPD)
- ☐ Medical patient currently at bed rest
- ☐ Leg plaster cast or brace
- ☐ Other risk factors_____

Each Risk Factor Represents 3 Points

- ☐ Age over 75 years
- ☐ Major surgery lasting 2-3 hours
- ☐ BMI > 50 (venous stasis syndrome)
- ☐ History of SVT, DVT/PE
- ☐ **Family history of DVT/PE**
- ☐ Present cancer or chemotherapy
- ☐ Positive Factor V Leiden
- ☐ Positive Prothrombin 20210A
- ☐ Elevated serum homocysteine
- ☐ Positive Lupus anticoagulant
- ☐ Elevated anticardiolipin antibodies
- ☐ Heparin-induced thrombocytopenia (HIT)
- ☐ Other thrombophilia
  Type_____

Each Risk Factor Represents 2 Points

- ☐ Age 60-74 years
- ☐ Major surgery (> 60 minutes)
- ☐ Arthroscopic surgery (> 60 minutes)
- ☐ Laparoscopic surgery (> 60 minutes)
- ☐ Previous malignancy
- ☐ Central venous access
- ☐ Morbid obesity (BMI >40)

Each Risk Factor Represents 5 Points

- ☐ Elective major lower extremity arthroplasty
- ☐ Hip, pelvis or leg fracture (< 1 month)
- ☐ Stroke (< 1 month)
- ☐ Multiple trauma (< 1 month)
- ☐ Acute spinal cord injury (paralysis)(< 1 month)
- ☐ Major surgery lasting over 3 hours

For Women Only (Each Represents 1 Point)

- ☐ Oral contraceptives or hormone replacement therapy
- ☐ Pregnancy or postpartum (<1 month)
- ☐ History of unexplained stillborn infant, recurrent spontaneous abortion ($\geq$ 3), premature birth with toxemia or growth - restricted infant

Total Risk Factor Score ☐

VTE Risk and Suggested Prophylaxis

Total Risk Factor Score	Incidence of DVT	Risk Level	Prophylaxis Regimen**
0-1	<10%	Low Risk	No specific measures; early ambulation.
2	10-20%	Moderate Risk	LWMH, UFH (5000U BID), ES, or IPC.
3-4	20-40%	High Risk	LMWH, UFH (5000U TID), or IPC.
5 or more	40-80% - 1-5% mortality	Highest Risk	Pharmacological: LMWH*, UFH, Warfarin*, or in combination with ES or IPC.

Legend

ES- Elastic Stockings
IPC- Intermittent Pneumatic Compression
UFH- Unfractionated Heparin
LMWH- Low Molecular Weight Heparin

* Use for major orthopedic surgery
** For the appropriate prophylaxis is in a particular patient, check with your consultant concerning best method and dose.

Choice of VTE prophylaxis: _____ Duration: _____ Days: _____

Signature_____Date_____

Based on: Geerts WH et al: Prevention of Venous Thromboembolism. Chest 2004;126(suppl 3):338S-400S; Nicolaides AN et al: 2001 International Consensus Statement: Prevention of Venous Thromboembolism, Guidelines According to Scientific Evidence.; Arcelus JI, Caprini JA, Traverso CI. International perspective on venous thromboembolism prophylaxis in surgery. Semin Thromb Hemost 1991; 17(4):322-5.; Borow M, Goldson HJ. Postoperative venous thrombosis. Evaluation of five methods of treatment. Am J Surg 1981;141(2):245-51.; Caprini JA, Arcelus I, Traverso CI, et al . Clinical assessment of venous thromboembolic risk in surgical patients. Semin Thromb Hemost 1991;17(suppl 3):304-12.; Caprini JA, Arcelus JI et al: State-of-the-Art Venous Thromboembolism Prophylaxis. Scope 2001; 8: 228-240.; Caprini JA, Arcelus JI, Reyna JJ. Effective risk stratification of surgical and nonsurgical patients for venous thromboembolic disease.*Seminars in Hematology*, April 2001;38(2)Suppl 5:12-19.; Caprini, JA. Thrombosis risk assessment as a guide to quality patient care, Dis Mon 2005;51:70-78.; Oger E: Incidence of Venous Thromboembol ism: A Community-based Study in Western France. Thromb Haemost 2000; 657-660.; Turpie AG, Bauer KA, Eriksson BI, et al. Fondaparinux vs. Enoxaparin for the Prevention of Venous Thromboembolism in Major Orthopedic Surgery: A Meta-analysis of 4 Randomized Double-Blind Studies. Arch Intern Med 2002; 162(16):1833--40.; Ringley et al: Evaluation of intermittent pneumatic compression boots in congestive heart failure. American Surgeon 2002; 68(3): 286-9.; Morris et al. Effects of supine intermittent compression on arterial inflow to the lower limb. Archives of Surgery 2002. 137(11):1269-73.; Sugarman HJ et al, Ann Surg: 234 (1) 41-46, 2001

Venous thromboembolism

MAIN OBJECTIVES OF TREATMENT

- Reduction of fatality
- Prevention of recurrence
- Prevention of late sequelae

PULMONARY EMBOLISM and DVT TREATMENT

INITIAL

Thrombolytic treatment

Heparin (UFH or LMWH)

Oral anticoagulant therapy (OAT) and new antithrombotics

LONG -TERM

OAT and new antithrombotics
LMWH

HOME

OAT and new antithrombotics

LMWH

TREATMENT OF VTE

***HEPARIN(UFH)??:80u/kg loading>18u/kg/hr**
PTT 1.5-2.5

OR

***HEPARIN(LMW):**

1mg/kgx2 enoxaparin

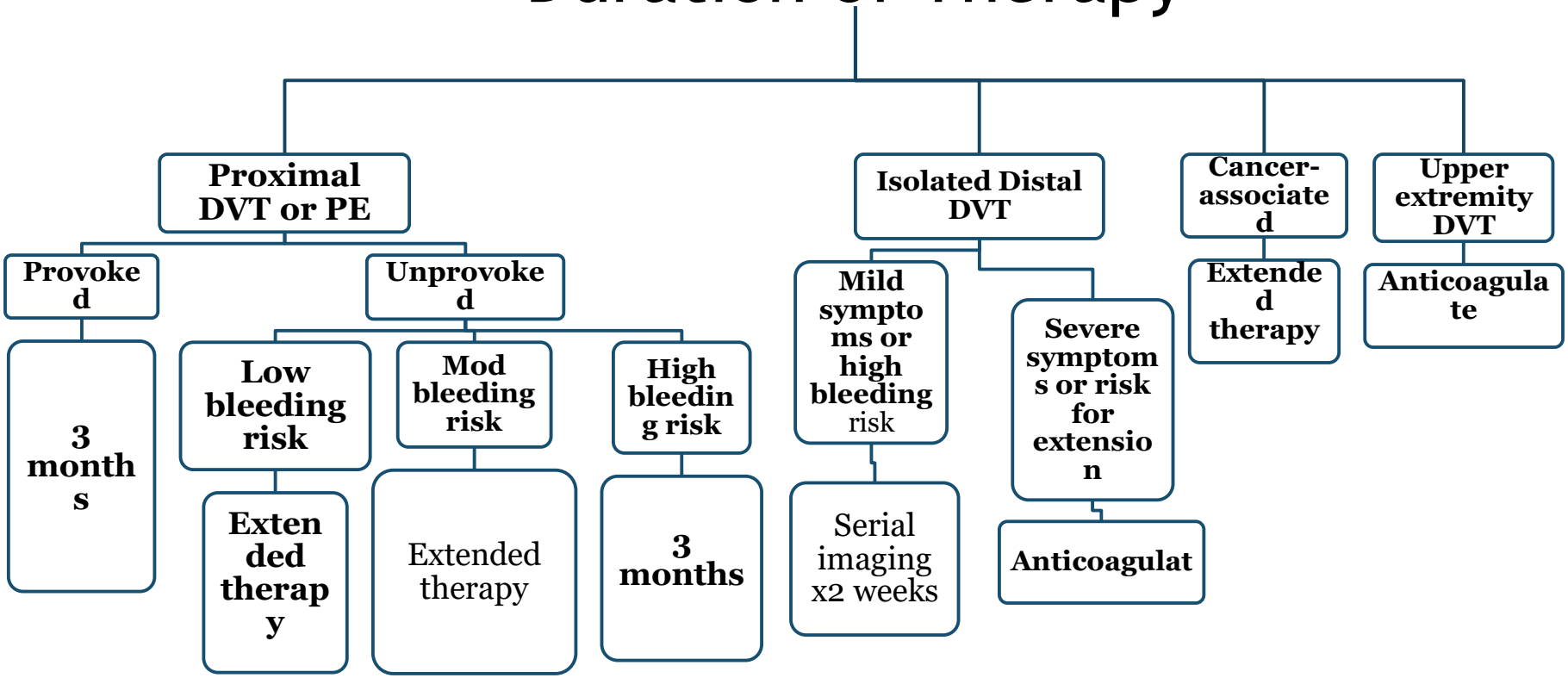
175u/kgx1 tinzaparin

***WARFARIN: start with 5mgx1 keep INR 2-3**

OVERLAP HEPARIN+WARFARIN

*** OR NEW ORAL ANTICOAGULANTS**

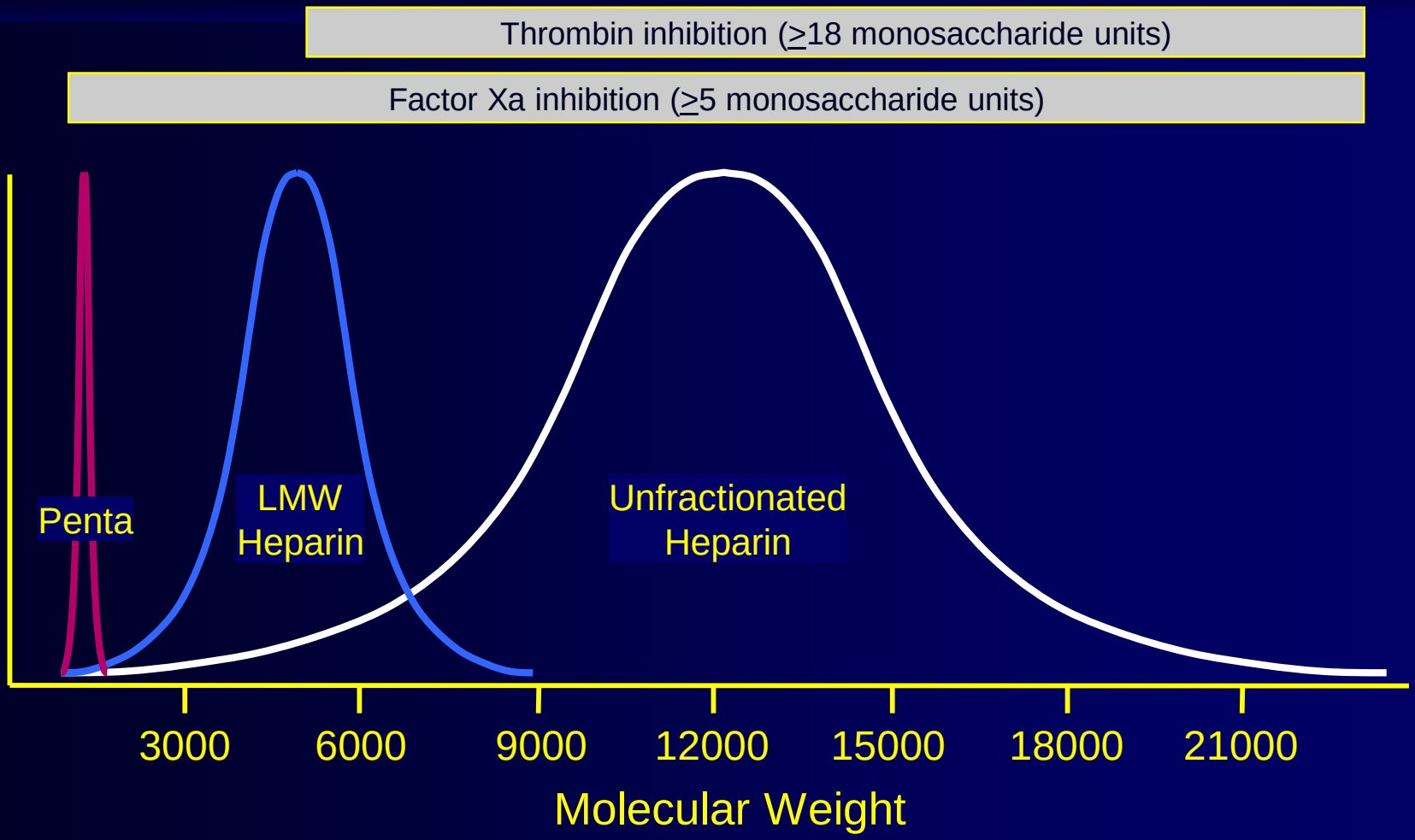
Duration of Therapy



VTE:OTHER TREATMENT MODALITIES

*THROMBOLYTIC THERAPY
* V.Thrombectomy
*IVC Filters
*Pulmonary embolectomy
*Post DVT syndrome

Heparin Preparations Used Clinically



Warfarin

Pharmacokinetics

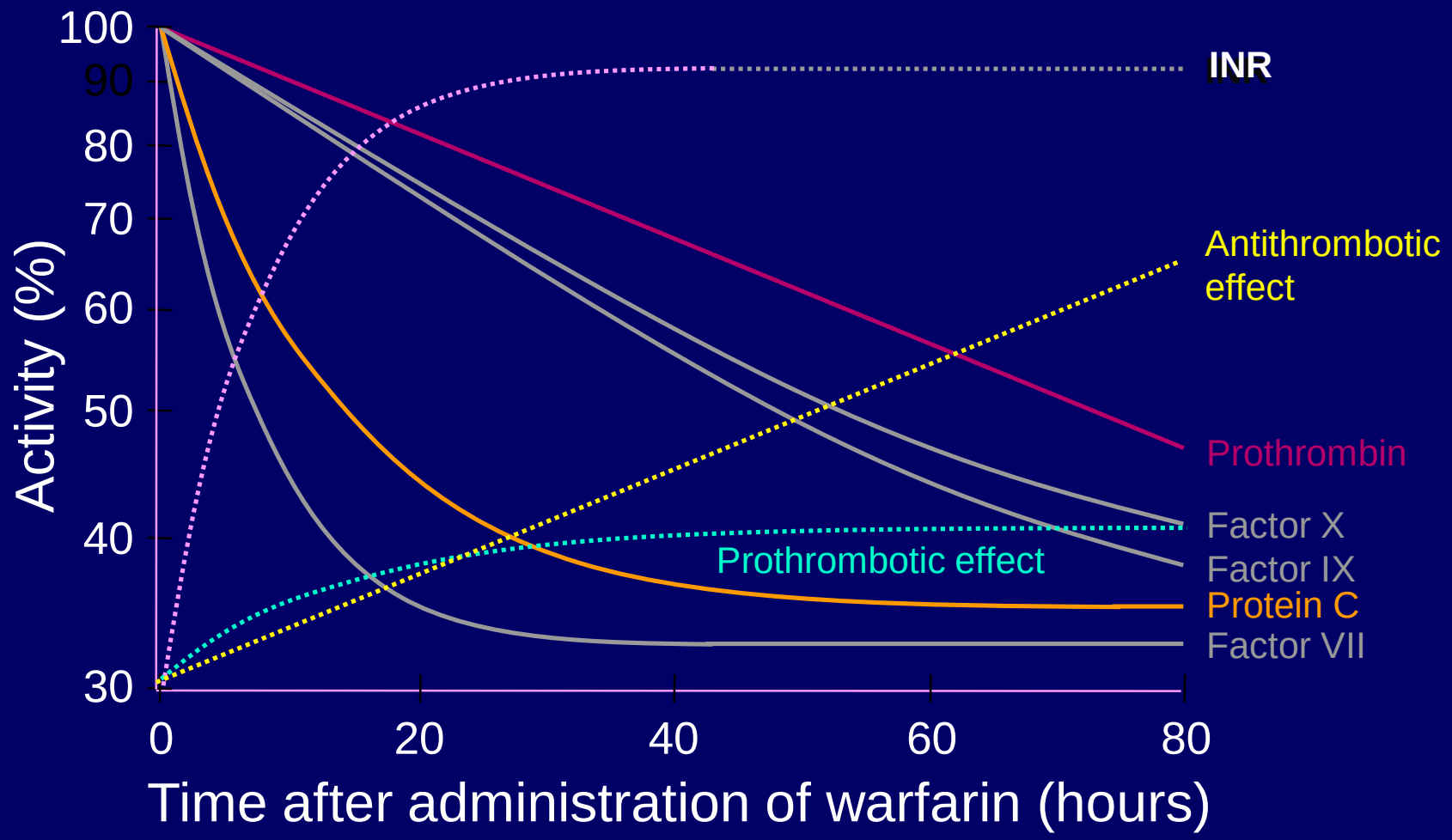
Plasma concentration peaks 2-8 h after an oral dose
99% bound to plasma proteins (albumin)
Half-life in plasma ~25-60 h

Inhibits biosynthesis of vitamin K-dependent zymogens (delayed onset of action)

Prothrombin(II)
Factor VII
Factor IX
Factor X
} procoagulant

Protein C
Protein S
} anticoagulant

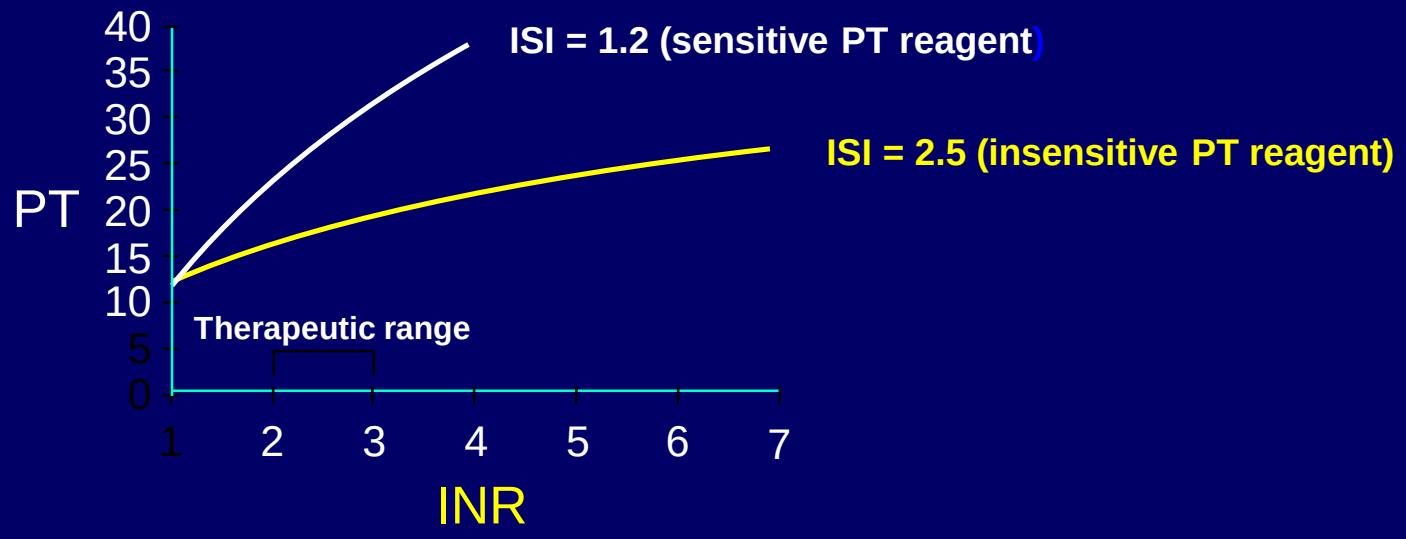
Clearance of Vitamin K-dependent Proteins



International Normalized Ratio (INR)

$$INR = \left(\frac{\text{Patient PT}}{\text{Control PT}} \right)^{C}$$

C = International Sensitivity Index



Complications of Warfarin Therapy

Bleeding

Birth defects and abortion

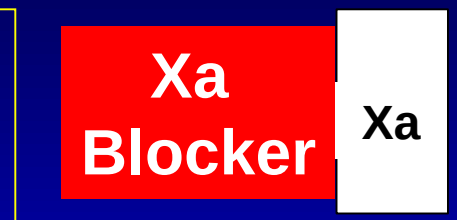
Contraindicated during pregnancy

Skin necrosis
Microvascular thrombosis
In patients with heterozygous protein C or S deficiency if a high initial dose is used or heparin overlap is inadequate

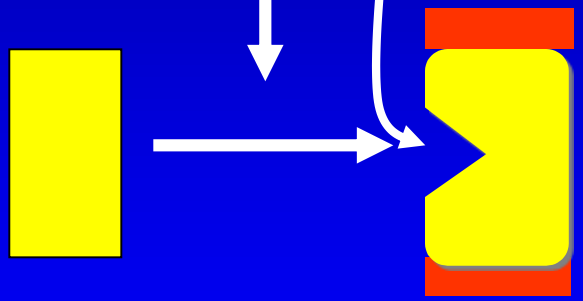
Common Pathway

New Oral Anticoagulants

Apixaban
Rivaroxaban



Dabigatran

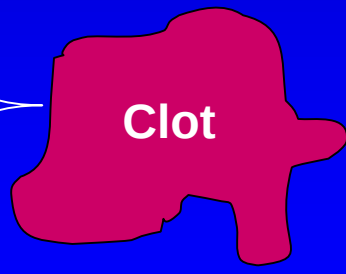


Prothrombin
FII

Thrombin

Fibrinogen

Fibrin



NOAC indications include:

- Reduces risk of stroke in non-valvular atrial fibrillation
- Prevention of VTE following hip or knee replacement
- Treatment and ongoing prevention of VTE

Contraindications to NOAC therapy include:

- Renal impairment
  - a reduced dose may be used in moderate renal impairment, depending on renal function, NOAC and indication
- Disorders of haemostasis
- Clinically significant active bleeding
- Prosthetic heart valve
- Liver disease
- Pregnant and breastfeeding women
- Children under 18 years

Ruxolitinib in the treatment of MPN

Selective JAK I & II inhibitor

Second line after hydroxyurea

Offers improvement of systemic symptoms, trx requirements.

No survival benefit as yet