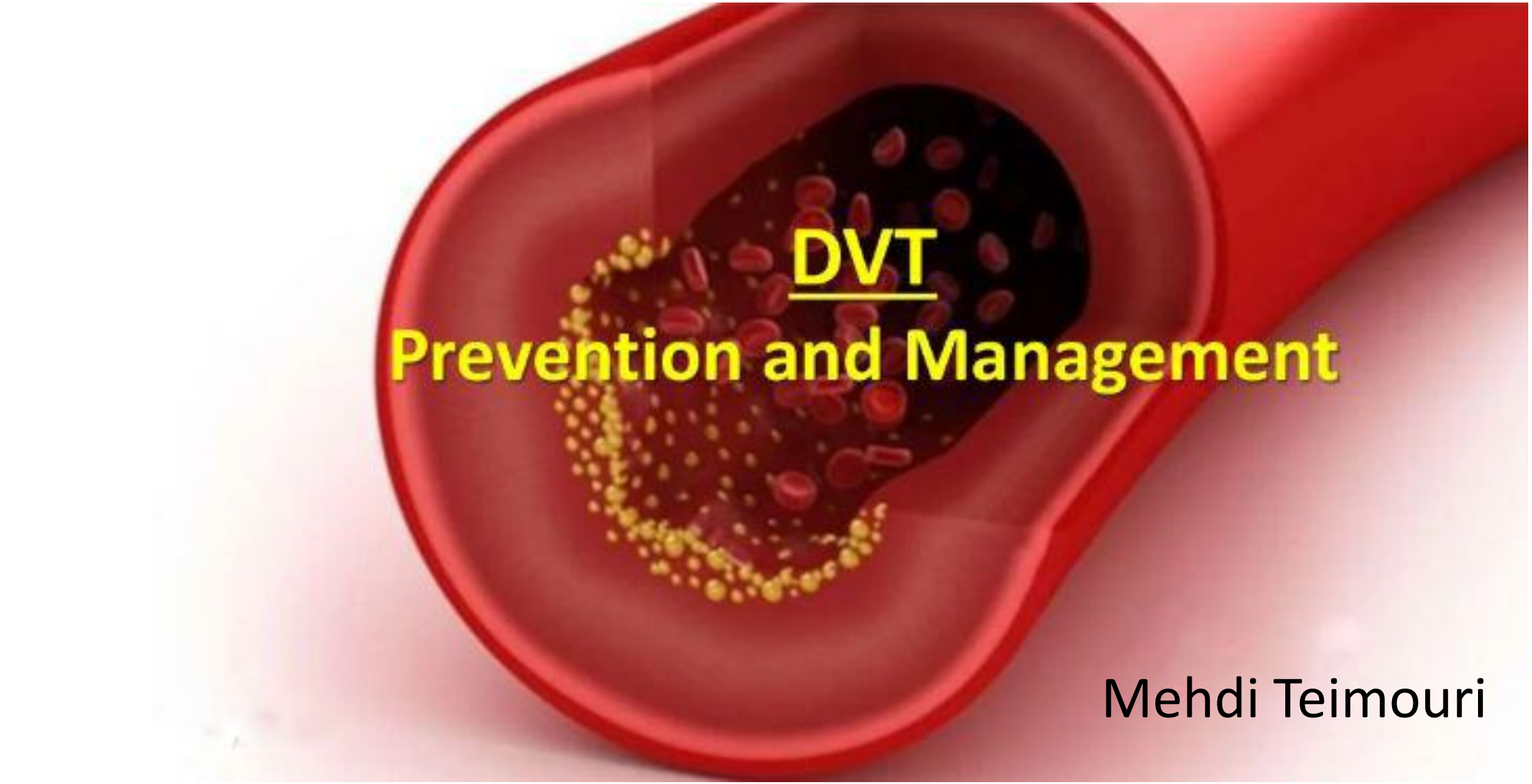

Mehdi Teimouri


Autre miracle.
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Raoul auctier
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die auquel environ laage
de viii ans lui survint en
la cheville de son pie une en
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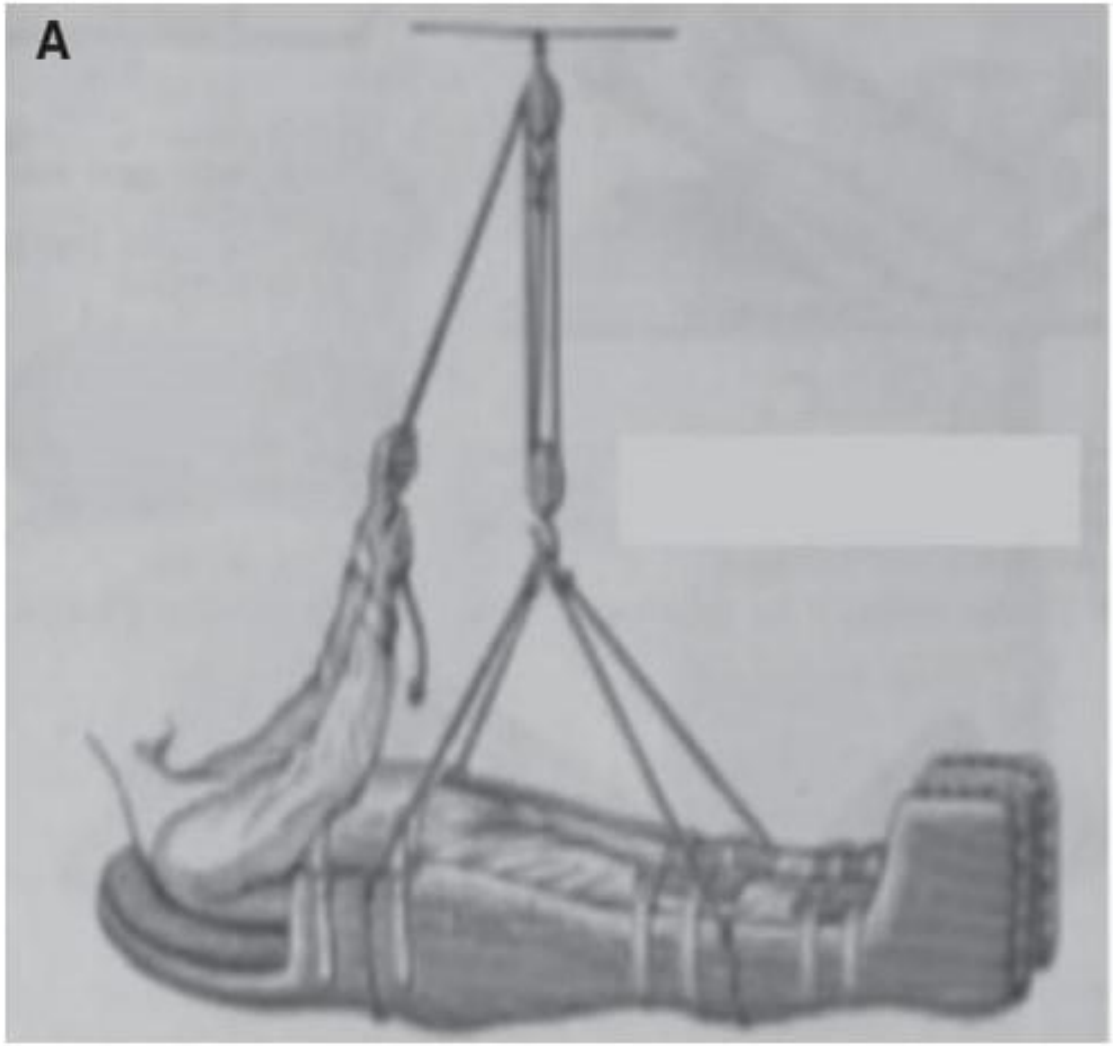


B

NOUVEAU LIT METALLIQUE DEMONTABLE
A MOUVEMENTS VARIABLES RAINAL FRERES

(Vente et location)

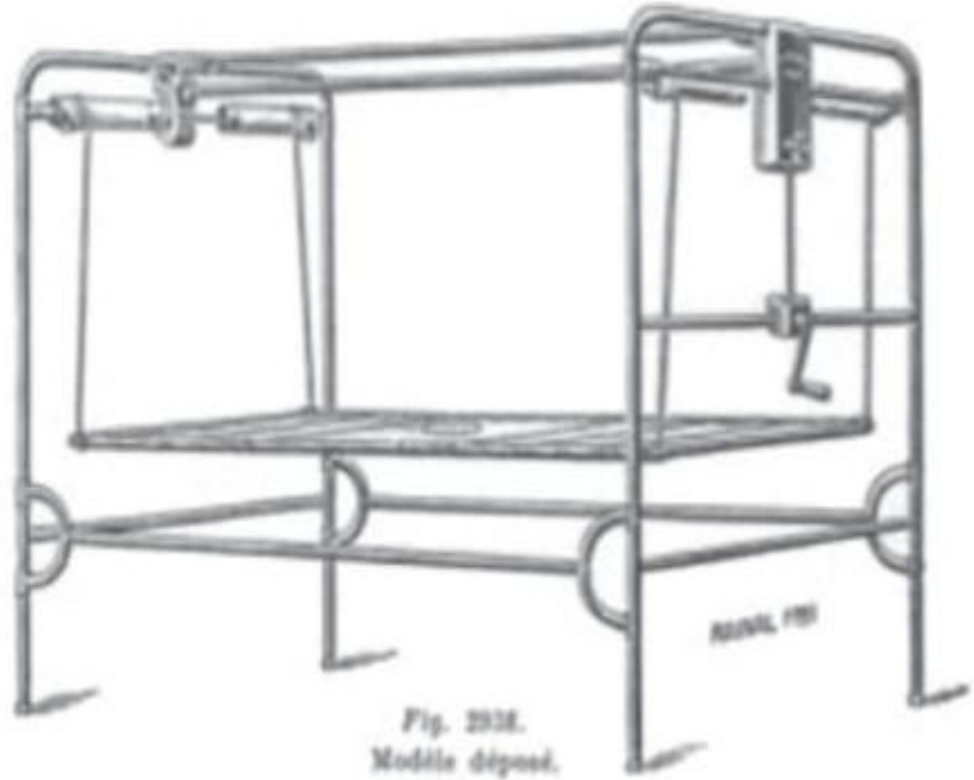
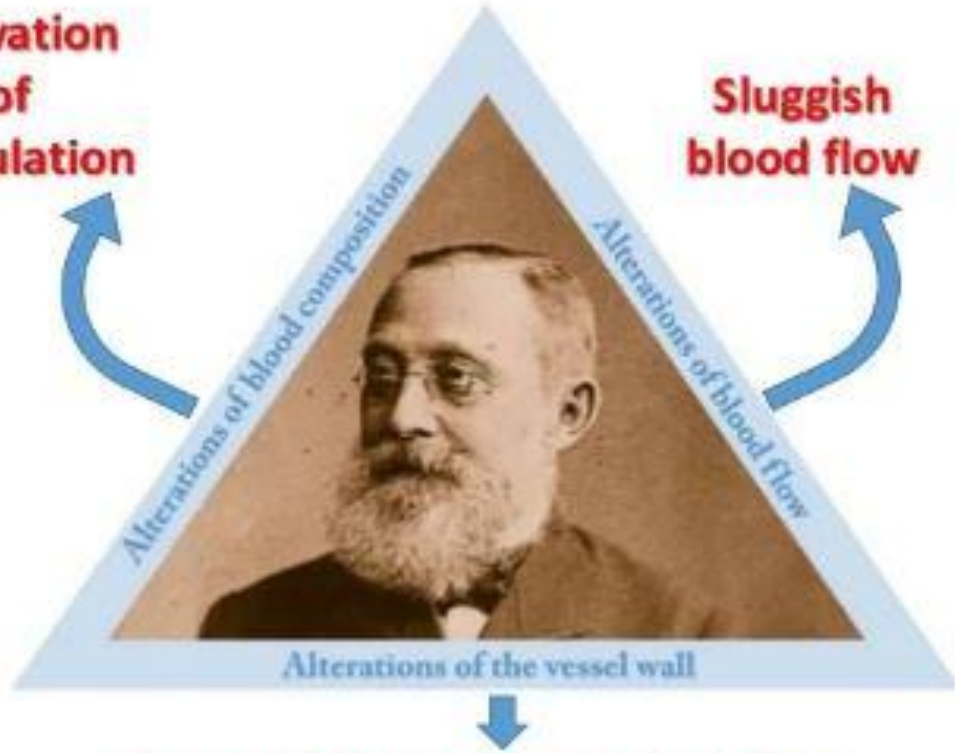


Fig. 2938.
Modèle déposé.


KILL-RATS!
STOP
THIS ROBBI
Rat Killer
WARFARIN



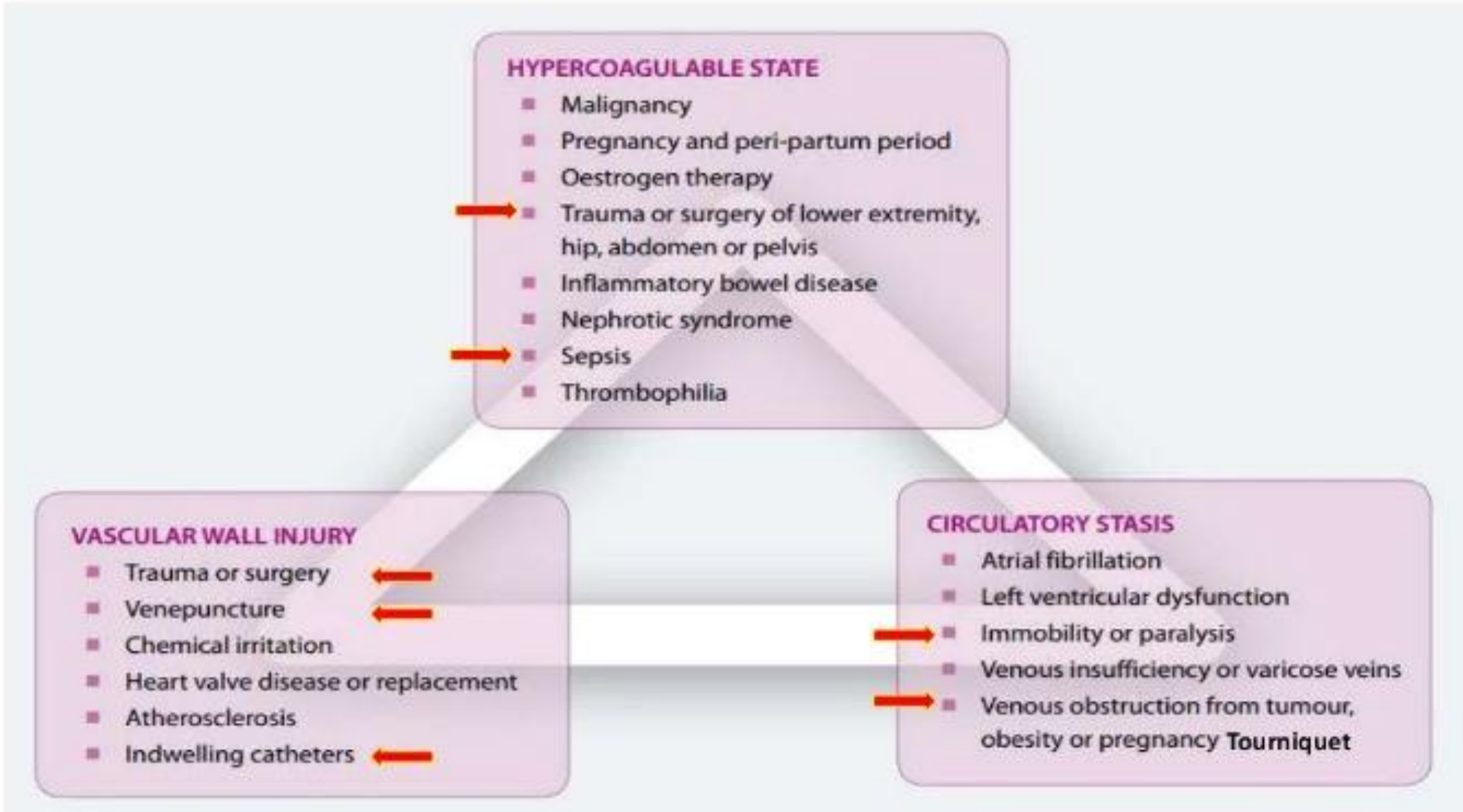
Orthopedic Surgery and DVT

THE LINK

- Pre-op Immobilization (stasis)
- Trigger of tissue factor
  - reamed products (THR)
  - tissue debris ,fat → activation of coagulation
- Distortion of Femoral and Poplietal viens
  - retraction,twisting,manipulation - damage to vessel wall
- Prolonged post-op Immobilization.

Anticlotting mechanism - Antithrombin III (ATIII)

Surgery / Trauma → **Reduction in circulating ATIII** → Clotting process starts.
Decrease in ATIII is greater, and remains for longer in THA than in cases of general surgery.

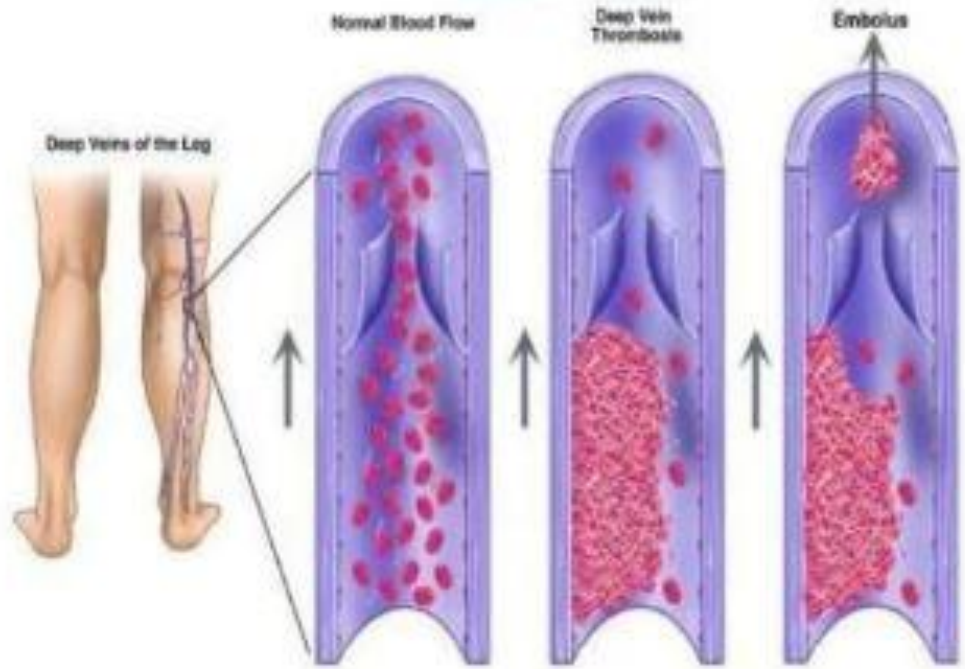

HYPERCOAGULABLE STATE
Malignancy
Pregnancy and peri-partum period
Oestrogen therapy
Trauma or surgery of lower extremity, hip, abdomen or pelvis
Inflammatory bowel disease
Nephrotic syndrome
Sepsis
Thrombophilia
VASCULAR WALL INJURY
Trauma or surgery
Venepuncture
Chemical irritation
Heart valve disease or replacement
Atherosclerosis
Indwelling catheters
CIRCULATORY STASIS
Atrial fibrillation
Left ventricular dysfunction
Immobility or paralysis
Venous insufficiency or varicose veins
Venous obstruction from tumour, obesity or pregnancy Tourniquet

The Problem

Table 1 – Absolute risk of DVT in hospitalized patients.

Group of patients	Prevalence (%) DVT
Clinical patients	10–20
General surgery	15-40
Major gynecological surgery	15-40
Major urological surgery	15-40
Neurosurgery	15-40
Stroke	20-50
Arthroplasties of the hip or knee	40-60
Spinal cord injury	60-80
Major trauma	40-80
Critical patients	10-80

Rates based on DVT in patients not receiving thromboprophylaxis.
Source: Adapted from Geerts WH, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(Suppl 3):338S-400S.



The Problem

Prevalence of DVT, as Detected by Venography After Total Joint Arthroplasty and Hip Fracture Repair, in the Absence of Prophylaxis. Pulmonary Embolism Rates Were Derived From Studies That May Have Used Thromboprophylaxis[1]

	DVT, %		PE, %	
Procedure	Total	Proximal	Total	Fatal
THA	42-57	18-36	0.9-28	0.1-2.0
TKA	41-85	5-22	1.5-10	0.1-1.7
HFS	46-60	23-30	3-11	0.3-7.5

Abbreviations: DVT, deep vein thrombosis; HFS, hip fracture surgery; PE, pulmonary embolism; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Post-thrombotic syndrome

Develops in **20 - 50%** of patients after symptomatic DVT. Can also develop after asymptomatic DVT
Chronic pain, swelling, heaviness, varicose veins and venous ulcers.

VTE & Orthopaedic Surgery

ASYMPTOMATIC DVT
Venographically proven

20 - 40 % of inpatients undergoing THA and TKA

JBJS(Am) 1998. Ciccone WJ, II, Fox PS, Neumyer M, Rubens D, Parrish WM, Pellegrini VD., Jr ***Ultrasound surveillance for asymptomatic deep venous thrombosis after total joint replacement.***

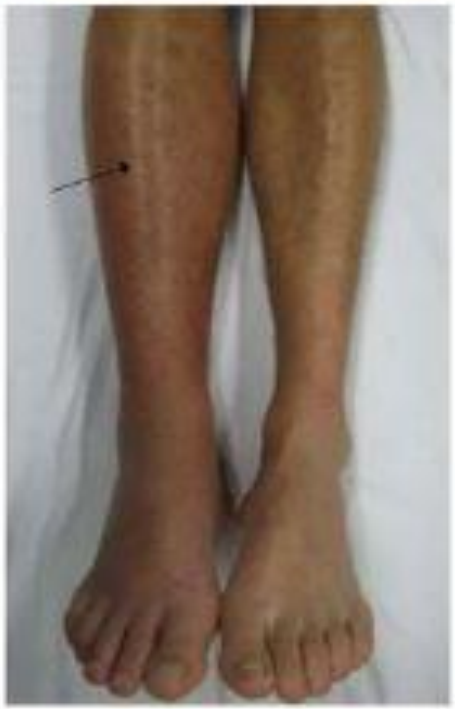
Clinical significance of asymptomatic DVTs ??

A very low correlation between the presence of DVTs and PEs

J Arthroplasty 2010. Parvizi J, Jacovides CL, Bican O, et al. ***Is deep vein thrombosis a good proxy for pulmonary embolus?***

Many asymptomatic thrombi regress spontaneously without treatment, without extending or evolving to PE or PTS

SYMPTOMATIC DVT



Only 1 in 8 thrombi identified by venography evolve to symptomatic DVT.

Proximal thrombi (above poplipteal vein) - higher likelihood of being symptomatic.

PULMONARY EMBOLISM

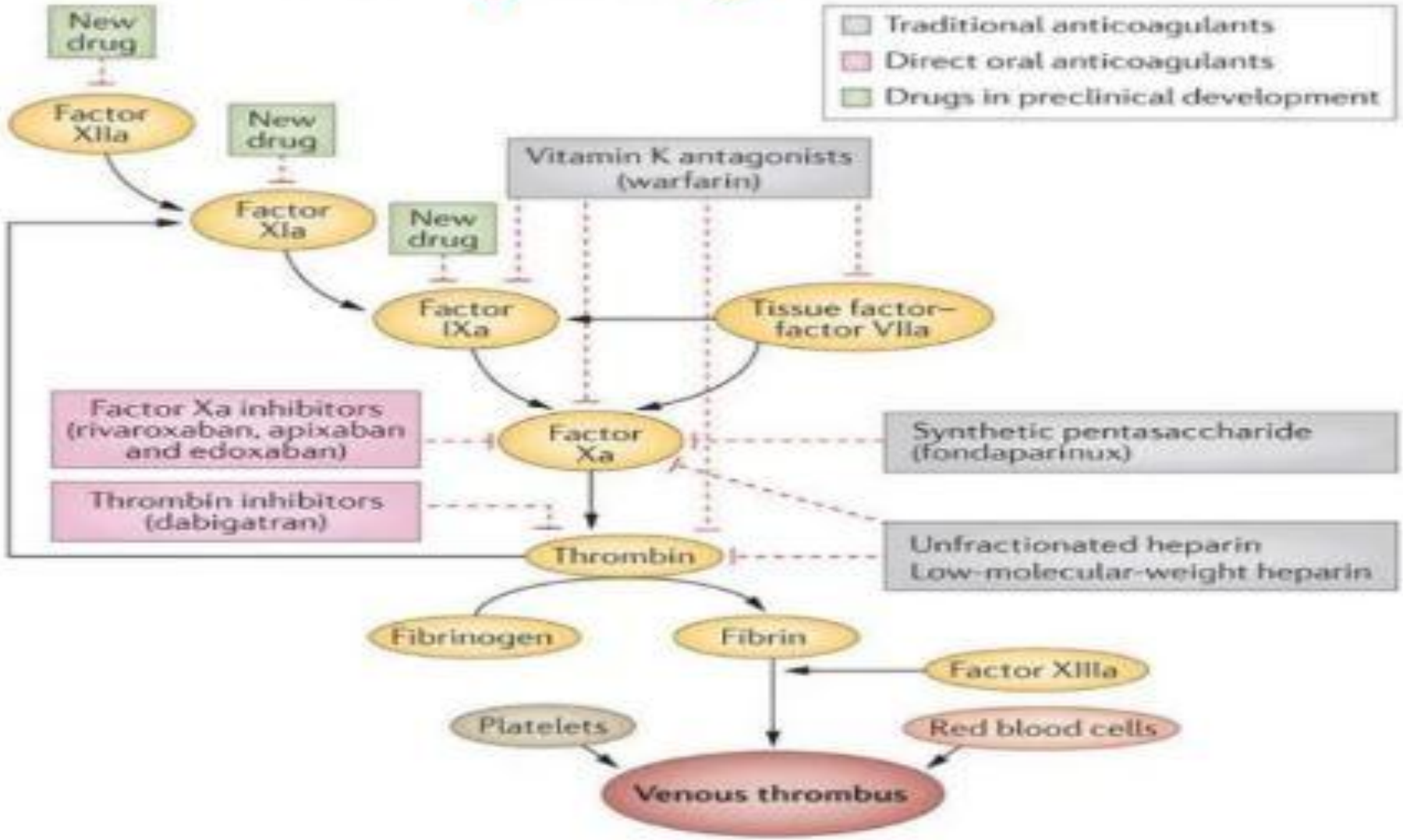
80% patients who develop PE will have no evidence of peripheral venous thrombosis before presenting with PE.

Chest 1995. Stein PD, Henry JW. ***Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy.***

Symptomatic PE is rare after THA and TKA

3 - 4% of all symptomatic cases of VTE evolve to fatal PE

Pharmacological Agents for VTEP



VTEP GUIDELINES

3 clinical guidelines on prophylaxis of VTE for THA and TKA

AMERICAN COLLEGE OF CHEST PHYSICIANS

SCIP Surgical Care Improvement Project
A National Quality Partnership

AAOS
American Academy of Orthopaedic Surgeons

A clinical guideline is not a protocol for patient care or a statement of dogma immune to disagreement or change.

Nor is a guideline a substitute for sound clinical judgment.

Several decades of experience and hundreds of clinical studies → Still **no consensus** on the ideal method of thromboprophylaxis for patients undergoing THA and TKA.

Many patients are at risk for insufficient prophylaxis or excessive bleeding risks.

AMERICAN COLLEGE OF CHEST PHYSICIANS

ACCP - 16,500 members → Pulmonology, critical care medicine, sleep medicine, cardiology, cardiothoracic surgery, pediatric pulmonology, and pediatric critical care medicine.

1986 - ACCP first VTE guidelines; Most recent (9th) edition was published in 2012.

DVT, detected by venography or USG, was the primary outcome measure (based on prevalence) in the development of these guidelines.

ACCP guidelines have **advocated for prevention of DVT (both symptomatic and asymptomatic)** as an important surrogate marker for prevention of clinically significant outcomes

Surgical patients are categorized as "low," "medium," or "high" risk, but all THA and TKA patients are considered high risk, regardless of patient age, activity level, or comorbidities.

AMERICAN COLLEGE OF CHEST PHYSICIANS

CAUSE FOR CONCERN

ACCP emphasize prophylaxis with strong pharmacologic agents.

The strongest recommendations are **based on prospective randomized studies**, with most of these **comparing the efficacy and safety of 1 pharmacologic agent with another or with placebo**.

Only data from prospective randomized studies were used to make a grade 1A recommendation.
Thus, a grade 1A recommendation could not be based on data from even large (>1000 patients) cohort studies.

Prospective randomized studies of pharmacologic agents include only carefully selected patients with few comorbidities
→ Guidelines may not be applicable to the wide spectrum of patients undergoing THA or TKA.

Few studies evaluated mechanical or multimodal (combined) prophylaxis.

ACCP underestimate the risks related to the use of anticoagulants.

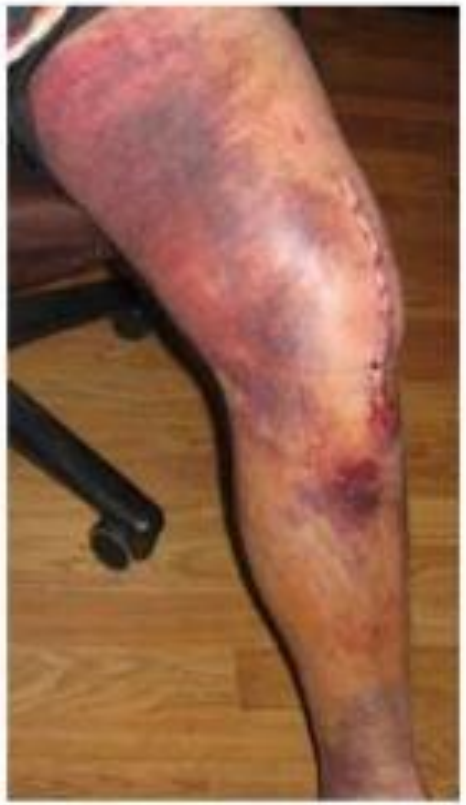
ACCP guidelines were more focused on efficacy, often under emphasizing the risk of bleeding, which is associated with serious complications including hematoma, infection, and reoperation.

Orthopedists' Concerns With ACCP Guidelines

ACCP described a major bleeding episode as overt bleeding associated with at least 1 of the following:

- Death or life threatening clinical event
- Bleeding confirmed as retroperitoneal, intracranial or intraocular
- Transfusion of > 2 PRBCs or whole blood
- Decrease of Hb > 2 g/dL compared with relevant postoperative level

These criteria generally do not apply to THA and TKA patients.



Dramatic increase in bleeding after adopting ACCP protocols.

J Arthroplasty 2006. Keeney JA, Clohisy JC, Curry MC, Maloney WJ. ***Efficacy of combined modality prophylaxis including short-duration warfarin to prevent venous thromboembolism after total hip arthroplasty.***

J Arthroplasty 2008. Novicoff WM, Brown TE, Cui Q, et al. ***Mandated venous thromboembolism prophylaxis: possible adverse outcomes.***

Patients with wound complications requiring reoperation within 30 days of TKA were 10 times more likely to have subsequent major surgery and associated morbidities than those without.

JBJA (Am) 2009. Galat DD, McGovern SC, Larson DR, et al. ***Surgical treatment of early wound complications following primary total knee arthroplasty.***

Orthopedists' Concerns With ACCP Guidelines

Numerous potential financial conflicts of interest were found with many authors.

The Institute of Medicine issued recommendations regarding guideline development that discouraged any financial conflict of interest among its authors of clinical guidelines

PLoS ONE 2012. Norris SL, Holmer HK, Burda BU, Ogden LA, Fu R. ***Conflict of interest policies for organizations producing a large number of clinical practice guidelines.***

Historically AAOS and ACCP have disagreed on the appropriateness of Aspirin for pharmacologic VTE prophylaxis in orthopaedic surgery.

Orthopaedic surgeons were also prohibited from using less aggressive and less expensive options such as aspirin with mechanical compression devices, even in young patients with a very low VTE risk.

Orthopedists' Concerns With ACCP Guidelines

Symptomatic PE is relatively rare after THA or TKA.

90-day rate of **fatal PE - 0.22%** after 44,785 TKAs and 0.15% after 27,000 TKAs in the Scottish Registry.

JBJS (Br) 2005. Howie C, Hughes H, Watts AC. ***Venous thromboembolism associated with hip and knee replacement over a ten-year period: a population-based study.***

Review of > 200,000 TKAs in a California database, the 90-day rate of **symptomatic PE was 0.41%.**

JBJS (Am) 2006. SooHoo NF, Lieberman JR, Ko CY, Zingmond DS. ***Factors predicting complication rates following total knee replacement.***

Risk of serious bleeding complications

290 patients (THA and TKA) given the ACCP grade 1A-recommended **10-day course of LMWH**

- **Major bleeding occurred in 9% of patients**, with 4.7% requiring readmission.
- Efficacy of this approach was also questioned, in that symptomatic DVT occurred in 3.8% of patients and nonfatal symptomatic PE occurred in 1.3%.

J Arthroplasty 2007. Burnett RS, Clohisy JC, Wright RW, et al. ***Failure of the American College of Chest Physicians-1A protocol for Lovenox in clinical outcomes for thromboembolic prophylaxis.***

Patients who return to OR within 30 days after TKA for evacuation of a postoperative hematoma are at significantly increased risk for development of deep infection or for requiring other major surgery.

JBJS (Am) 2008. Galat DD, McGovern SC, Hanssen AD, Larson DR, Harrington JR, Clarke HD. ***Early return to surgery for evacuation of a postoperative hematoma after primary total knee arthroplasty.***

AAOS
American Academy of Orthopaedic Surgeons

2007 - Due to many concerns raised regarding the ACCP guidelines, the AAOS formed its DVT/PE workgroup and issued its own recommendations by reviewing the available literature on VTE with ***symptomatic DVT, PE, and mortality as endpoints***.

The goal was to achieve more balance between minimizing risk and maximizing efficacy, while minimizing conflicts of interest during the guideline development.

Patients were classified based on their medical history to identify their risk of VTE and bleeding.

2009 Ed

- For the first time, included aspirin monotherapy as VTE Prophylaxis.
- **Aspirin monotherapy - 325 mg BD**, beginning on the day of surgery and continued for **6 weeks *for patients without preoperative elevated VTE risk***.

AAOS has strongly lobbied for the **use of only symptomatic and/or fatal PE or death** as the primary outcomes to be addressed

AAOS 2011 and ACCP 2012

AAOS guidelines were in conflict with the ACCP guidelines until the 9th Ed of the ACCP recommendations (2012)

2012 Ed ACCP

- An entire chapter was devoted to the prevention of VTE in orthopaedic surgery patients.
- ACCP addressed almost all the concerns found in their previous clinical guidelines.
- Methodology was changed dramatically to focus on more symptomatic and significant outcomes like bleeding and wound drainage.

Inclusion of LDUFH and Aspirin

For the first time ACCP included daily full-dose **Aspirin (>300 mg) as acceptable chemoprophylactic monotherapy after total joint arthroplasty.**

ACCP advised using Aspirin, LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, LDUFH, VKA (grade 1B recommendations; strong recommendation, moderate-quality evidence) for **a minimum of 10–14 days** following joint replacement surgery, with **LMWH as the preferred agent.**

Chest 2012. Guyatt GH, Norris SL, Schulman S, Hirsh J, Eckman MH, Akl EA, Crowther M, Vandvik PO, Eikelboom JW, McDonagh MS, et al. ***Methodology for the development of antithrombotic therapy and prevention of thrombosis guidelines: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines***.

A statistically significant increase in ASA monotherapy prescriptions after the convergence of AAOS and ACCP CPG

Risk Benefit of Potent Anticoagulants

2001 - FDA approved **Fondaparinux** for VTEP after hip and knee replacement surgery.
RCT - Fondaparinux more effective in preventing VTE than enoxaparin (30 U BID) in patients undergoing elective major knee surgery, but with ***an increased risk of major bleeding***.

2011 - The FDA approved **Rivaroxaban** for VTEP after hip and knee replacement surgery.
RECORD 3 and RECORD 4 RCTs - Rivaroxaban superior to enoxaparin for VTEP after TKA, with similar bleeding rates.

2014 - FDA approved **Apixaban** for VTEP after hip and knee surgery.
ADVANCE-2 RCT - Apixaban a convenient and more effective alternative to Lovenox (LMWH) after TKA without increased bleeding risk.

NO Xa inhibitor reversal agent is a major concern for clinicians.

Delicate balance between efficacy and safety

Risk Benefit of Potent Anticoagulants

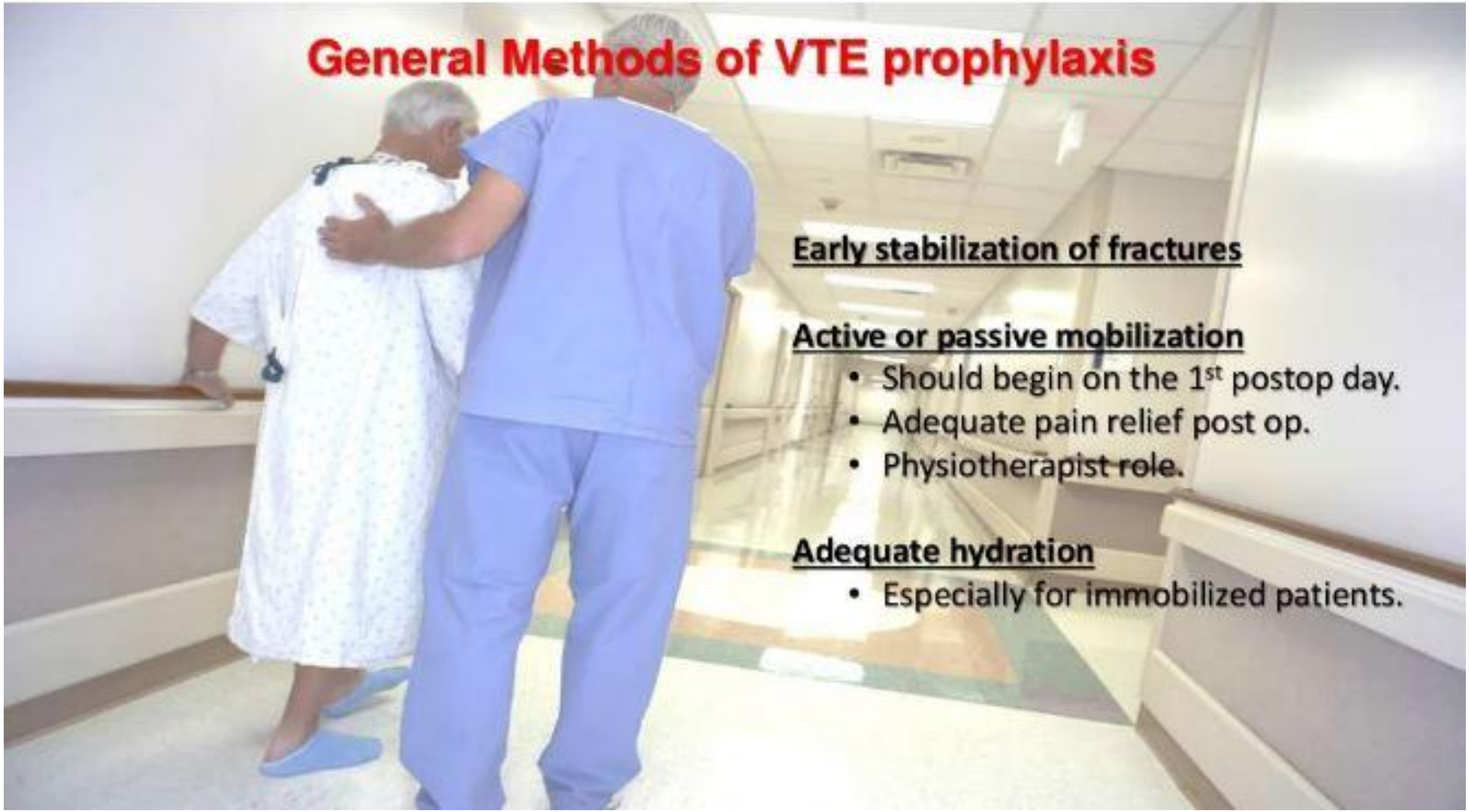
Evidence supporting the increased risk of more potent anticoagulants *became available during or after 2014.*

J Arthroplasty 2015. Mostafavi Tabatabaee R, Rasouli MR, Maltenfort MG, Parvizi J. ***Cost-effective prophylaxis against venous thromboembolism after total joint arthroplasty: warfarin versus aspirin.***

J Arthroplasty 2015. Huang R, Buckley PS, Scott B, Parvizi J, Purtill JJ. ***Administration of aspirin as a prophylaxis agent against venous thromboembolism results in lower incidence of periprosthetic joint infection.***

Clin Orthop Relat Res 2014. Raphael IJ, Tischler EH, Huang R, Rothman RH, Hozack WJ, Parvizi J. ***Aspirin: an alternative for pulmonary embolism prophylaxis after arthroplasty?***

General Methods of VTE prophylaxis



Early stabilization of fractures

Active or passive mobilization

- Should begin on the 1st postop day.
- Adequate pain relief post op.
- Physiotherapist role.

Adequate hydration

- Especially for immobilized patients.

Mechanical Methods of VTE prophylaxis

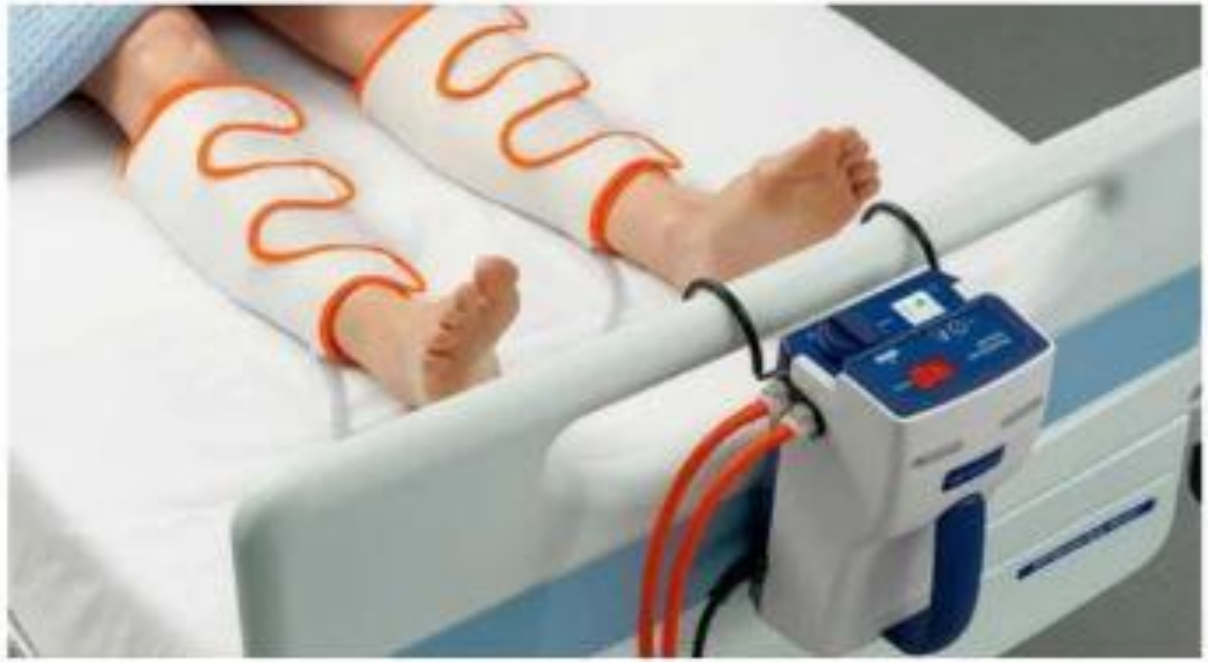
IPCD

ACCP guidelines - Use of IPCD for least **18 h / day**

- As an **adjunct** to chemoprophylaxis
- Or in patient with high risk of bleeding .

AAOS guidelines

- Use **in patients with known bleeding disorders**, such as hemophilia or active liver disease
- As with chemoprophylaxis in patient with previous VTE



Multicenter RCT – IPCD vs Enoxaparin

- **IPCD was just as effective as enoxaparin** in preventing proximal and distal DVT and PE events, but resulted in a much lower bleeding risk (1.3 % IPCD vs 4.3 % LMWH).
- Disclosure - 1 or more of its authors or immediate family received benefits from the commercial party.

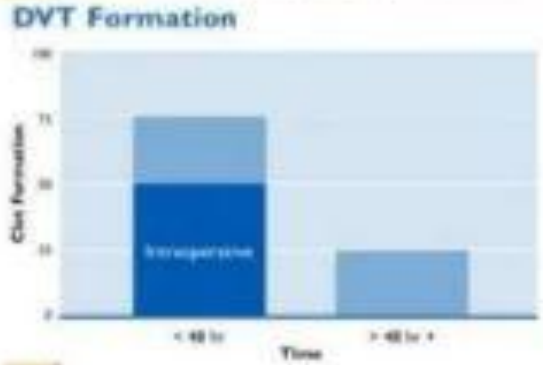
JBJS (Am) 2010. Colwell CW, Jr, Froimson MI, Mont MA, et al. ***Thrombosis prevention after total hip arthroplasty: a prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin.***

Mechanical Methods of VTE prophylaxis

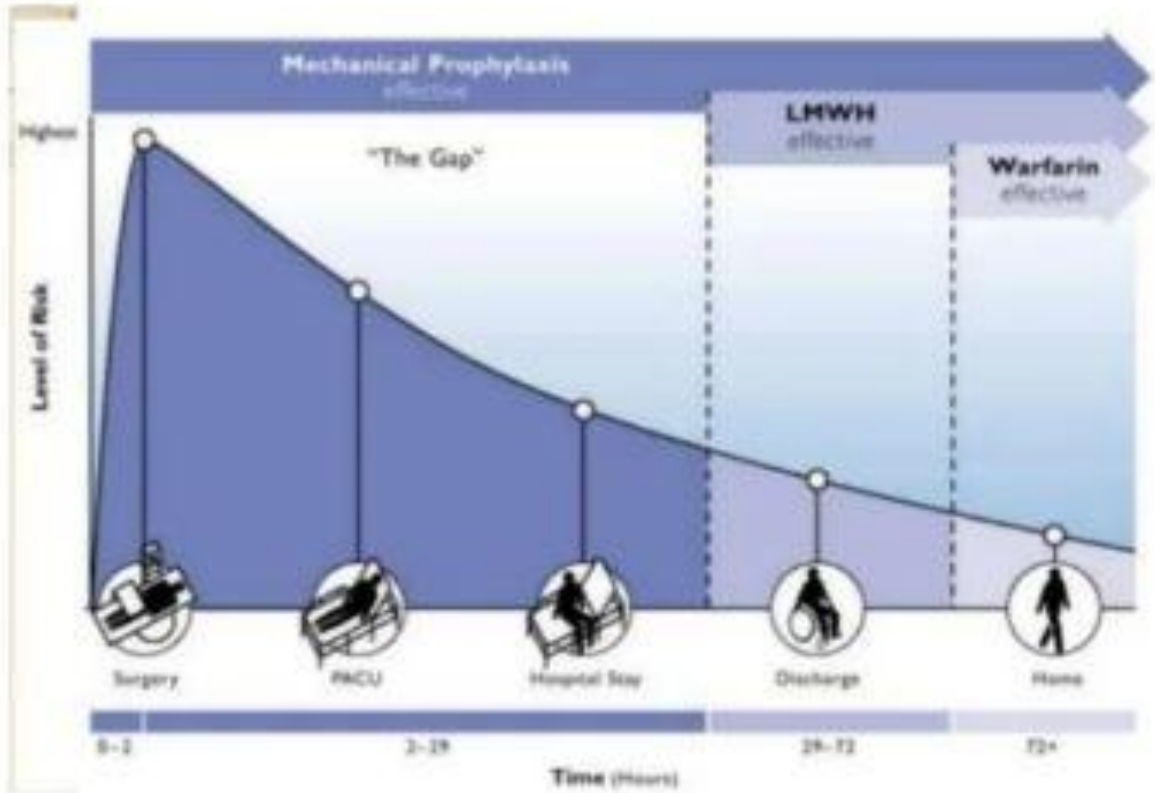
Graduated Compression Stockings

THE GAP IN PROTECTION

The "Gap" in protection is when the patient is at risk for DVT, but the administration of pharmacological prophylaxis cannot begin.



50% of thrombi formation begins intraoperatively



Pharmacological VTE prophylaxis

Aspirin

Pulmonary Embolism Prevention (PEP) trial - Concluded that low-dose aspirin for 35 days, results in 7 times less symptomatic DVT cases, but in 3 bleeding cases and 2 nonfatal myocardial infarction per 1000 patients.

In the current edition of ACCP guidelines, aspirin is indicated as a prophylaxis option – although not typically the agent of choice –in major orthopedic surgery.

2011 AAOS - **325 mg BD** in patients at increased risk for major bleeding and at standard or increased risk for PE.

Aspirin as part of Multimodal Prophylaxis

Multimodal prophylaxis has demonstrated efficacy in the reduction of VTE.

RCT - **Aspirin + Portable continuous enhanced circulation device** had a significantly lower rate of venographically detected or clinical DVT compared to LMWH (6.6% vs 28.5%, p = 0.002)

J Arthroplasty 2006. Gelfer Y, Tavor H, Oron A, Peer A, Halperin N, Robinson D. ***Deep vein thrombosis prevention in joint arthroplasties: continuous enhanced circulation therapy vs low molecular weight heparin.***

Pharmacological VTE prophylaxis

LMWH – Enoxaparin / Dalteparin

Anti-Xa activity, stronger as compared to UFH.

Reduced binding to plasma proteins and cells is responsible for more predictable dose-response relationship, longer T½ and lower complication:

Excreted by kidneys and do not require laboratory monitoring

Meta-analysis (16 RCTs) ***Enoxaparin vs newer anticoagulants*** (rivaroxaban, dabigatran, apixaban)
Newer anticoagulants are higher in efficacy, but also have higher risk of bleeding.

- Risk of symptomatic VTE was lower with rivaroxaban, and similar with dabigatran and apixaban.
- Rivaroxaban was associated with a significant increase in the risk of clinically relevant bleeding.
- Dabigatran did not show a significant increase compared with enoxaparin.
- Apixaban was associated with a significant reduction in risk of bleeding.

After balancing efficacy and safety (symptomatic DVT or PE with clinically relevant bleeding events), no significant difference was found between LMWH and newer anticoagulant agents.
All papers reviewed in this meta-analysis were ***sponsored by pharmaceutical companies***.

BMJ 2012. Outes GA, Fernandez AIT, Gea LS, Castrillon EV. ***Dabigatran, rivaroxaban, or apixaban vs enoxaparin for thromboprophylaxis after total hip or knee replacement: systematic review, meta-analysis, and indirect treatment comparison***.

Pharmacological VTE prophylaxis

VKAs / Warfarin

Warfarin vs LMWH as prophylaxis for TKA

Several multicentric studies showed that LMWH was a more effective agent to prevent DVT formation ($P < 0.05$), but no difference to warfarin in preventing symptomatic events including PE, in part since most of studies measured primary outcome as asymptomatic DVT.

LMWH resulted in more bleeding episodes compared with warfarin, although the difference is not significant ($P > 0.05$).

- ***Challenging to use in practice*** - Narrow therapeutic window, variability in dose-response, interaction with drugs and diet.
- Need a strict laboratory and clinical control to ensure efficacy and safety.
- A weekly INR monitoring aiming at a 2-3 INR value range.

Advantages - Oral route of administration and low price.

Pharmacological VTE prophylaxis

Factor Xa Inhibitors

Fondaparinux

A pentasaccharide with highly inhibitory effect on Factor Xa.

Long T½ 17-20 h that ensures a prolonged effect, but also the drawback of a lack of a quick reversibility.

Daily dose is 2.5 mg SC, the first dose at 6-8 h postoperatively.

PENTAMAX study - ***A higher rate of bleeding with Fondaparinux compared to Enoxaparin*** (2.1% versus 0.2%; P = 0.06), although Fondaparinux is superior to Enoxaparin in preventing VTE

Rivaroxaban

Selective oral Direct Factor Xa inhibitor - Inhibits not only free FXa, but also prothrombinase activity and clot-associated FXa activity.

It is well tolerated, has a rapid onset of action, a T½ about 5–9 h, and a predominantly renal excretion.

In a fixed, unmonitored, OD dose of 10 mg in the RECORD 1 and 2 trials for THA, and in the RECORD 3 and 4 for TKA, it proved to be a ***superior antithrombotic to Enoxaparin, and with similar rates of bleeding***.

Pharmacological VTE prophylaxis

Dabigatran etexilate

A direct inhibitor of thrombin.

Maximum effect within 2-3 h due to a rapid absorption and a T½ of 12-14 h.

Start with one 110 mg capsule at 1-4 h postoperatively and continue with 2 x 110 mg capsules OD.

Lower dose in patients over 75 years or with kidney problems, or in association with amiodarone, quinidine or verapamil.

Studies RE-MOBILIZE and RE-MODEL show a similar incidence of bleeding with Enoxaparin

Current clinical guidelines provide an orthopaedic surgeon with more latitude, and choices of VTE prophylaxis without emphasis on aggressive chemical, and often unneeded, prophylaxis.

Modern arthroplasty advocates early postoperative mobilization and use of mechanical prophylaxis in combination with chemoprophylaxis.

The key to determining the appropriate chemical prophylaxis for patients is to balance safety and efficacy while minimizing bleeding.

Need for a Hospital Policy for VTEP

Decision making related to VTE prophylaxis based on the combination of individual patients' risks and contraindications.

Hospital-approved VTE prophylaxis assessment tool.
Standardized prophylaxis based upon the patient's assessed status.

- Treating Clinician to conduct a VTE prophylaxis assessment of each hospitalized patient.
- Nursing Officer in charge to notify (and document notification) treating clinician with the results of the patient's VTE prophylaxis assessment status.
- Treating clinician to order VTE prophylaxis within 06 h of receiving notification of the patient's VTE prophylaxis assessment status.
- If the hospital's approved standard prophylaxis treatment is not ordered by treating clinician, the rationale must be documented in the medical record.

PROTOCOL

Structured risk assessment for Hospital Acquired Thrombosis should be carried out for all elective patients, both medical and surgical.

Target patient Population

(a) Adults (18 y and older) admitted to hospital as inpatients.
(b) In-patients with acute medical illness (MI, CVA, severe infection or exacerbation of COPD)
(c) Trauma inpatients, SCI
(d) Patients admitted to ICUs
(e) Cancer inpatients
(f) People undergoing long-term rehabilitation in hospital

Risk assessment for patients admitted in emergency

All medical and surgical patients, within 6 hrs of admission
Patients who are identified as having increased risk of HA Thrombosis must have thromboprophylaxis started pre-operatively where clinically appropriate.

Elective cases - Patients undergoing surgery will undergo risk assessment for VTE in the surgical OPD and reassessed within 12 hrs of admission to a hospital ward.

Part I - Caprini Risk Assessment Matrix

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)
- ☐ Ac 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 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 lower extremity arthroplasty
- ☐ Hip,Pelvis,leg Fracture (<1 month)
- ☐ Multiple trauma (< 1 month)
- ☐ Acute spinal cord injury (paralysis <1month
- ☐ Major Surgery lasting more than 3 hours

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_____

For Women only

Each Risk factor Represents 1 point

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

Total risk factor Score ☐

Part II - VTE Risk and Suggested VTEP

Total Risk Factor Score	Incidence of DVT	Risk Level	Recommended Prophylaxis
0-1	<10%	Low risk	No specific measures, early ambulation
2	10-20%	Moderate risk	GCS/IPC
3-4	20-40%	High Risk	GCS/IPC or LMWH-Inj Enoxaparin 40 mg daily OR tab Rivoraxaban 10 mg oral daily
5 or >	40-80% 1-5% mortality	Highest Risk	IPC + or LMWH-Inj Enoxaparin 40 mg daily OR tab Rivoraxaban 10 mg oral daily

All patients who are considered for pharmacoprophylaxis will undergo CBC including platelet count, serum creatinine and prothrombin time (INR).

Part III – VTEP Safety considerations

Factors associated with bleeding Which preclude use of anticoagulants	Local factors precluding mechanical prophylaxis
Is patient having or recently had any active bleeding?	Does patient have severe peripheral arterial disease?
Does patient have or had HIT?	Does patient have congestive heart failure?
Is patients platelet count less than 1,00,000/mm^3	Does patient have DVT/thrombophlebitis?
Is INR >1.5?	Does Patient have fracture or wound over the lower limb?
Is creatinine >2/creatinine clearance <30 ml/min? (requires modification of dose)	**If anyone yes → not a candidate for mechanical prophylaxis**
Is patient on anti-platelet agents or anticoagulants?	
If any one Yes → not a candidate for Pharmacological prophylaxis → consider GCS/IPC	

Part IV - VTEP Modality Chosen

- ❑ **Graduated Compression Stockings(GPC)**
- ❑ **Intermittent Pneumatic Compression(IPC)**
- ❑ **LMWH Inj Enoxaparin 40 mg SC daily**
- ❑ **LMWH inj Enoxaparin 30 mg SC daily (in patients with Cr clearance<30ml)**
- ❑ **Pregnant patients LMWH 30 mg SC daily till 20 weeks / 30 mg SC BD after 20 weeks**
- ❑ **Tab Rivoraxaban 10 mg OD**

Monitor anti FactorXa level in pregnancy

VTEP Monitoring

If LMWH prophylaxis is continued for more than 6 days then on the 7th day check:

- Potassium
- Platelets (if count has fallen by 50% without obvious explanation discuss with Chest physician)
- If heparin used within the preceding 100 days prior to starting treatment check Platelets after 24 hours.

VTEP Monitoring

Heparin Induced Thrombocytopenia (HIT) / skin lesions

- HIT usually presents between 5 and 14 days after starting therapy.
- Considered if platelet count falls below normal range, or to < 50% of baseline platelet count.

If HIT suspected, refer as emergency to haematology.
If patient develops thrombocytopenia, skin reaction or new thrombosis within 14 days of starting therapy, HIT should be considered.

Warfarin Induced Skin Necrosis

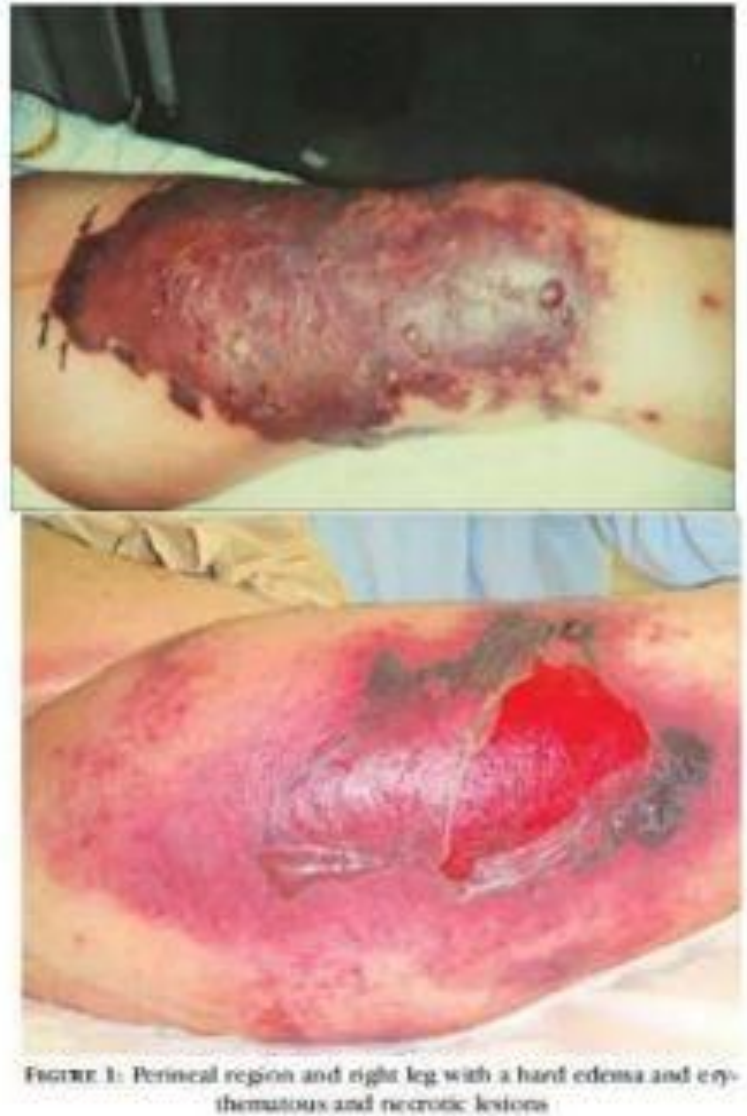


FIGURE 1: Perineal region and right leg with a hard edema and erythematous and necrotic lesions

VTEP for Orthopaedic Procedures

Elective Hip Arthroplasty

Inj LMWH (Enoxaparin 40 mg, started 12 h before surgery resumed 12 h after surgery and given for 5 days) followed by Tab Rivoraxaban 10mg for total period of **35 days**

Elective Knee Arthroplasty

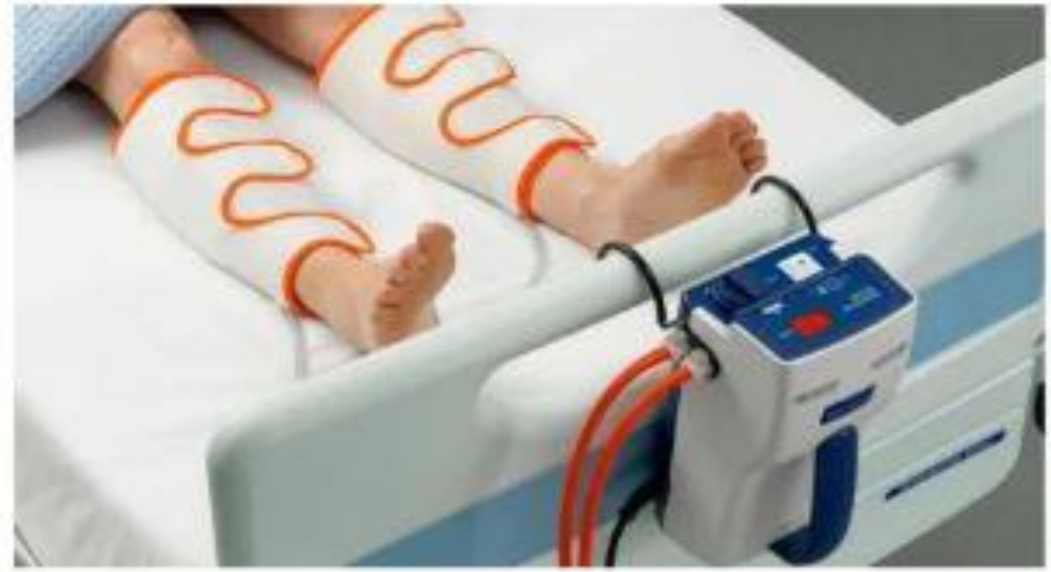
Inj LMWH (Enoxaparin 40 mg, started 12 h before surgery resumed 12 h after surgery and given for 5days) then Tab Rivoraxaban 10mg for a total period of **14 days**.

Hip, Pelvic and femur fractures

If surgery is delayed or in case of conservative management, LMWH is initiated during the time between hospital admission and surgery/ mobilization. inj LMWH Enoxaparin 40 mg SC daily is **given till patient is ambulant**.

Algorhythm for TKA / THA

At admission - Offer **IPC** → Continue Intra Op and Post Op



Contraindications for anticoagulation prophylaxis
→ Continue IPC only

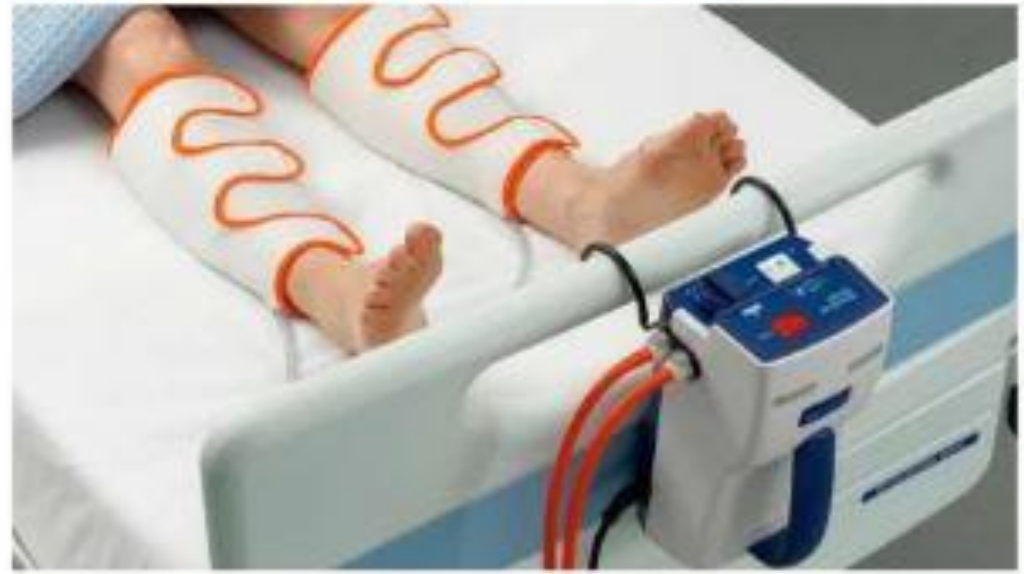
LMWH

- Start Inj Enoxaparin 40 mg SC 12 before surgery
- Restart within 12 h after surgery
- CBC, renal, hepatic function test and PT INR will be done before starting Inj Enoxaparin
- Continue for 5 days

All to get **Intra-op IPC**

Tab **Rivoraxaban** 10 mg OD from 6th post op day
(for 30 days for THA / 10 days for TKA)

Algorhythm for Hip / Pelvis / Femur fractures



At admission - Offer **IPC** → Continue Intra Op and Post Op

Contraindications for anticoagulation prophylaxis
→ Continue IPC only

LMWH

- Start Inj Enoxaparin 40 mg SC 12 before surgery
- Restart within 12 h after surgery
- CBC, renal, hepatic function test and PT INR will be done before starting Inj Enoxaparin
- Continue for 5 – 10 days

All to get **Intra-op IPC**

Tab **Rivoraxaban** 10 mg OD after stopping LMWH
(for 30 days / till ambulant)

INFORMED CONSENT FOR PHARMACOPROPHYLAXIS FOR VTE

Patient name:	Age/Sex:	Ward:
Relationship	Service No.:	Rank:
Name:	Unit	A &D No.:

I_____ have been assessed for risk for developing clotting in the veins and its effects (venous thromboembolism VTE) and my risk category has been assessed to be high/highest risk carrying risk of 20-40%/40-80% of developing VTE. I have been explained the meaning and effect of clot formation and its effects (VTE) in a language I understand. I have been advised to be given pharmacoprophylaxis to prevent VTE. I have been explained that drugs given for prevention of VTE may result in bleeding, wound haematoma, haemarthrosis.

Alternate methods of prevention of mechanical prophylaxis like graduated compression stockings and intermittent pneumatic compression devices have been explained to me and I understand that their effectiveness in prevention of VTE is less than that of pharmacoprophylaxis whereas there is no risk of bleeding.

I accept that all methods of prevention can only reduce the incidence of clotting and cannot guarantee total prevention of clotting and the risk of bleeding exist.

I request Dr_____ my treating clinician to proceed with pharmacoprophylaxis for VTE with Inj Enoxaparin/inj Fondaprinax/tab Rivoraxaban,

_____ _____

(Witness) Person giving consent

Relationship to patient if not the patient

Certified that I have explained to the patient the risks of VTE and methods of prevention and risk of pharmacoprophylaxis to the patient and NOK in a language they understand.

Date:

_____

Signature of treating clinician

Table 1. ACCP, SIGN, and AAOS guidelines for VTE prophylaxis for patients undergoing elective THR or TKR

Study	Guidelines	Clinical evidence (grade)	Duration of prophylaxis
ACCP (2008[19], 2012[31])	LMWH	1B	At least 10 to 14 days, and up to 35 days
	Low dose UFH	1B	
	VKA	1B	
	Fondaparinux	1B	
	Apixaban	1B	
	Dabigatran	1B	
	Rivaroxaban	1B	
	Aspirin	1B	
	IPCD	1C	
	Preference of LMWH to fondaparinux, apixaban, dabigatran, rivaroxaban, low dose UFH	2B	
	Preference of LMWH to VKA and aspirin	2C	
SIGN (2010, updated 2015[16])	LMWH In combination with mechanical prophylaxis Fondaparinux Rivaroxaban Dabigatran	A	Extended prophylaxis (grade A) Optimal duration of extended prophylaxis is unclear
	Aspirin is not recommended as a single pharmacologic agent for VTE prophylaxis	C	–
AAOS (2011[34])	Use of pharmacologic agents and/or mechanical methods	Moderate	–
	Unclear about which prophylactic strategy (or strategies) is/are optimal or suboptimal. No recommendation for or against specific prophylactics in these patients	Inconclusive	Patients and physicians discuss the duration of prophylaxis (consensus)

Table 2. NICE guidelines for VTE prophylaxis for patients undergoing elective THR or TKR

NICE study (2018[71])	Guidelines	Duration of prophylaxis
For patients undergoing elective THR	LMWH for 10 days and then aspirin	10 days LMWH Further 28 days aspirin
	LMWH in combination with anti-embolism stockings (until discharge)	28 days
	Rivaroxaban	>14 days
	Apixaban	
	Dabigatran	
For patients undergoing elective TKR	Aspirin (75 or 150 mg)	14 days
	LMWH in combination with anti-embolism stockings (until discharge)	14 days
	Rivaroxaban	>14 days
	Apixaban	
	Dabigatran	

Table 3. ACCP, SIGN, British Orthopaedic Association, and NICE guidelines for VTE prophylaxis for patients undergoing hip fracture surgery

Study	Guidelines		Clinical evidence (grade)	Duration of prophylaxis
ACCP (2008[19], 2012[31])	LMWH		1B	At least 10 to 14 days, and up to 35 days
	Low dose UFH		1B	
	VKA		1B	
	Fondaparinux		1B	
	Aspirin		1B	
	IPCD		1C	
	Preference of LMWH to fondaparinux, low dose UFH		2B	
	Preference of LMWH to VKA and aspirin		2C	
SIGN (2009[74])	In combination with mechanical prophylaxis	LMWH	A	4 weeks
British Orthopaedic Association (2007[75])		UFH	A	
		Fondaparinux	A	
	Aspirin is not recommended as a single pharmacological agent for VTE prophylaxis		D	–
NICE (2018[71])	LMWH		–	1 month
	Fondaparinux			

Table 4. Guidelines for VTE prophylaxis for patients undergoing various orthopaedic operations

Orthopaedic operation	Study	Guidelines	Clinical evidence (grade)/ Level of evidence
Knee arthroscopy	ACCP (2012[31])	No VTE prophylaxis rather than prophylaxis for patients undergoing knee arthroscopy without a history of prior VTE	2B
	Krych et al (2015[79])	Consider pharmacologic VTE prophylaxis for patients with a history of VTE, malignancy, or 2 or more classic risk factors	Level III (case-control study)
	NICE (2018[71])	LMWH for 14 days if: - total anaesthesia over 90 minutes or - VTE risk outweighs bleeding risk	
Isolated lower-leg injuries distal to the knee	ACCP (2012[31])	No VTE prophylaxis rather than pharmacological VTE prophylaxis in patients with isolated lower-leg injuries requiring leg immobilization	2C
Isolated foot and ankle surgery	Calder et al (2016[93])	Routine chemoprophylaxis is not indicated	A/Level II
	NICE (2018[71])	Consider pharmacological VTE prophylaxis if: - immobilization is required - total anaesthesia over 90 minutes or - VTE risk outweighs bleeding risk	
Cast immobilization	Testroote et al (2014[90]) Zee et al (2017[91])	LMWH for patients undergoing casting	Moderate-quality evidence
	NICE (2018[71])	LMWH or fondaparinux for patients whose VTE risk outweighs bleeding risk Consider stopping prophylaxis after 42 days	
Achilles tendon rupture	Patel et al (2012[92])	Routine use of VTE prophylaxis might be unwarranted	Level III
	Calder et al (2016[93])	Routine use of mechanical anti-VTE methods	B/Level II
Upper limb surgery	NICE (2018[71])	VTE prophylaxis is generally not needed if patients receive local or regional anaesthesia Consider VTE prophylaxis if: - total time under general anaesthesia over 90 minutes - difficulty to mobilize due to operation	–
Shoulder arthroplasty	Day et al (2015[94])	Mechanical prophylaxis combined with aspirin Pharmacological prophylaxis with agents other than aspirin may be warranted in patients with a demonstrated risk of VTE	Epidemiologic study (database analysis with survey of experts)

Table 5. ACCP (2008[19]) guidelines for VTE prophylaxis for patients undergoing spine surgery and those with a spine injury

Spine surgery/injury	Guidelines	Clinical evidence (grade)
Elective spine surgery with no additional thromboembolic risk factors	Early and frequent ambulation No routine use of other types of VTE prophylaxis	2C
Elective spine surgery with additional thromboembolic risk factors or an anterior surgical approach	Low dose UFH	1B
	LMWH	1B
	Optimal use of peri-operative IPC	1B
	GCS	2B
Elective spine surgery with multiple risk factors for VTE	Combination of a pharmacological method with the optimal use of a mechanical method	2C
Acute SCI	Routine VTE prophylaxis	1A
	LMWH after primary haemostasis	1B
	IPC and low dose UFH	1B
	IPC and LMWH	1C
	No use of low dose UFH alone	1A
Acute SCI with contraindication of pharmacologic VTE prophylaxis agents because of high bleeding risk	Optimal use of IPC and/or GCS	1A
	When the high bleeding risk decreases, pharmacological VTE prophylaxis substituted for or added to the mechanical VTE prophylaxis	1C
Incomplete SCI associated with evidence of a spinal haematoma on CT or MRI	Mechanical prophylaxis instead of pharmacological agents, at least for the first few days after the injury	1C
SCI	Against the use of an IVC filter for VTE prophylaxis	1C
Patients undergoing rehabilitation following acute SCI	Continuation of LMWH	1C
	Conversion to an oral VKA (INR target, 2.5; range, 2.0 to 3.0)	

Most common risk factors in pediatric patients
Central venous catheter
Congenital heart disease
Immobilization
Obesity
Oral contraceptives
Malignancy (eg, leukemia)
Prematurity
Surgery, especially orthopedic
Systemic infection
Trauma
Other risk factors
Heart failure
Inflammatory bowel disease
Certain cancer therapies (eg, asparaginase)
Personal or family history of thrombosis
Inherited thrombophilia: • Factor V Leiden mutation • Prothrombin G20210A mutation • Protein S deficiency • Protein C deficiency • Antithrombin deficiency
Antiphospholipid syndrome
Nephrotic syndrome
Pregnancy
Severe liver disease

++

Reviparin^Δ	**Infants <5 kg:** 150 units/kg/dose SubQ every 12 hours **Infants and children ≥5 kg:** 100 units/kg/dose SubQ every 12 hours	**Infants <5 kg:** 50 units/kg/dose SubQ every 12 hours **Infants and children ≥5 kg:** 30 units/kg/dose SubQ every 12 hours
Tinzaparin^Δ	**Infants 0 to 2 months:** 275 units/kg/dose SubQ daily **Infants 2 to 12 months:** 250 units/kg/dose SubQ daily **Children 1 to 5 years:** 240 units/kg/dose SubQ daily **Children 5 to 10 years:** 200 units/kg/dose SubQ daily (maximum 18,000 units/dose) **Children and adolescents 10 to 16 years:** 175 units/kg/dose SubQ daily (maximum 18,000 units/dose)	**Infants and children 1 month to 17 years:** 50 units/kg/dose SubQ daily
Dose titration (for therapeutic anticoagulation only)◇		
Anti-factor Xa level	Dose titration	Time to repeat anti-factor Xa level
<0.35 units/mL	Increase dose by 25%	4 hours after next dose
0.35 to 0.49 units/mL	Increase dose by 10%	4 hours after next dose
0.5 to 1 unit/mL	Keep same dose	Repeat the next day (4 hours after dose) If stable, can go to weekly monitoring
1.1 to 1.5 units/mL	Decrease dose by 20%	Before next dose
1.6 to 2 units/mL	Hold dose for 3 hours, then decrease dose by 30%	Before next dose, then 4 hours after next dose
>2 units/mL	Hold all doses until anti-factor Xa is 0.5 units/mL, then decrease dose by 40%	Before next dose and every 12 hours until anti-factor Xa is <0.5 units/mL

Periop management of patients on antiplatelet agents

Patients with coronary stents

Elective surgery postponed if aspirin and clopidogrel therapy must be discontinued

- Bare metal stents: 06 weeks
- Drug-eluting stents: 06 months

If surgery cannot be postponed, continue aspirin throughout perioperative period

Patients at high risk for cardiac events (exclusive of coronary stents)

- Continue aspirin throughout the perioperative period
- Discontinue clopidogrel at least 5 d (and preferably 10 d) before surgery
- Resume clopidogrel 24 hrs postoperatively

Patients at low risk of cardiac events

- Discontinue antiplatelet therapy 7-10 d before surgery
- Resume antiplatelet therapy 24 hrs postoperative

Management of Acute DVT

Anticoagulant therapy

- First episode of DVT → 3-6 months. Depending on site of thrombosis and on the ongoing presence of risk factors.
- Recurrent episodes → at least 1 year.
- Life long - Recurrent DVT/ chronic hypercoagulable state / life threatening PE

Risk of bleeding complications < 12%.
Although anticoagulation inhibits propagation, it does not remove the thrombus

Mostly as Outpatient

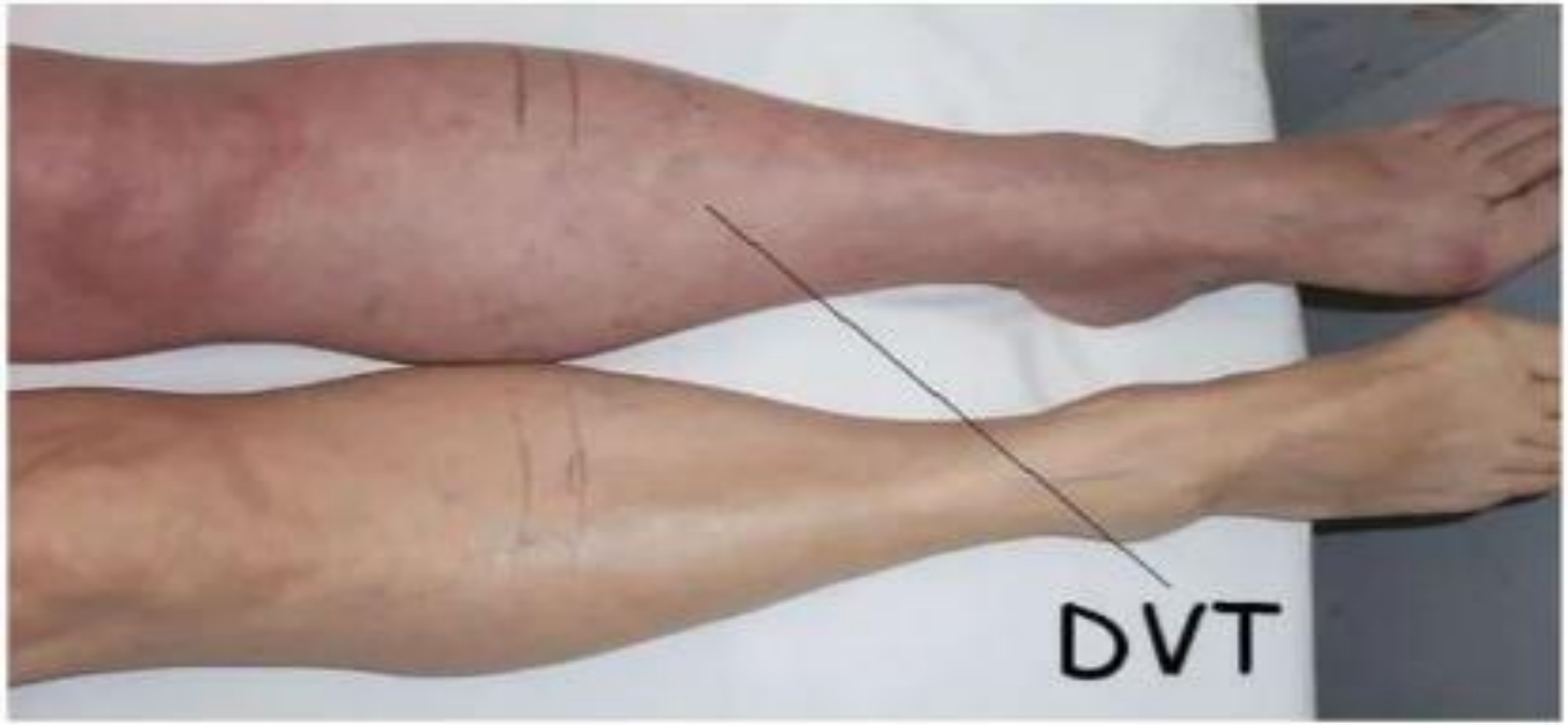
In-patients (Orthopaedic surgery patients)
Start with LMWH / Fondaparinux → Warfarin 5 mg PO daily is initiated and overlapped for 5 days until the INR is therapeutic >2 for at least 24 hours.

- Patients treated with LMWH or fondaparinux do not require monitoring of the aPTT.
- LMWH should be discontinued if the platelet count falls below 75,000

Management of Acute DVT

Ambulation as tolerated

- Early ambulation on day 2 after initiation of outpatient anticoagulant therapy + Effective compression is strongly recommended.
- Early ambulation without ECS is not recommended.



Management of Acute DVT

Bleeding risk on Anticoagulant therapy

LMWH

- Discontinue drug - Half-life of LMWH longer (4-6 h) than heparin.
- FFP / Platelet transfusions are ineffective.

- For severe hemorrhage ICH / GI Bleed) → **Antidote - Protamine** may be used, but it only reverses 60% of the drug's effects. 1 mg for every 100 units. Protamine should be administered at the same time that the infusion is stopped.

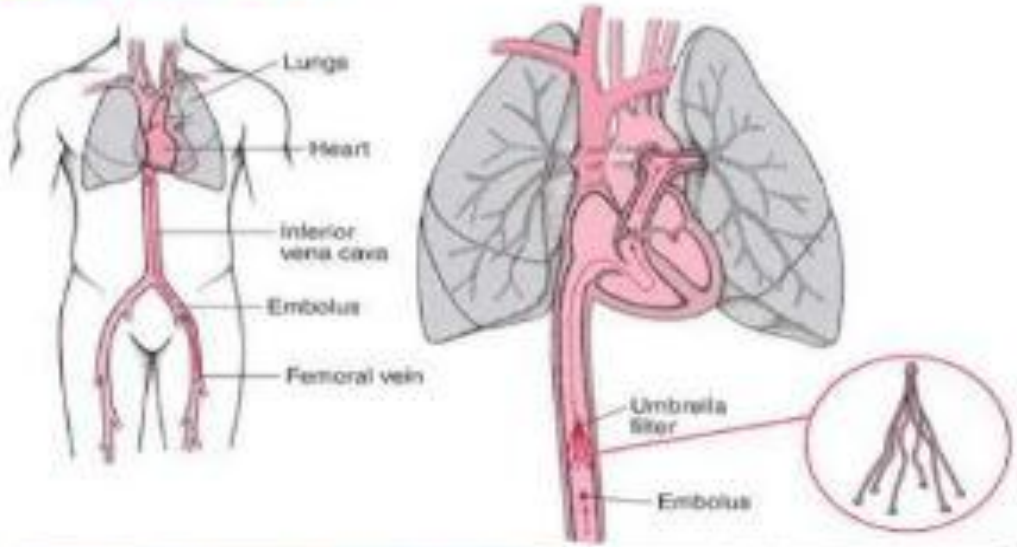
Warfarin

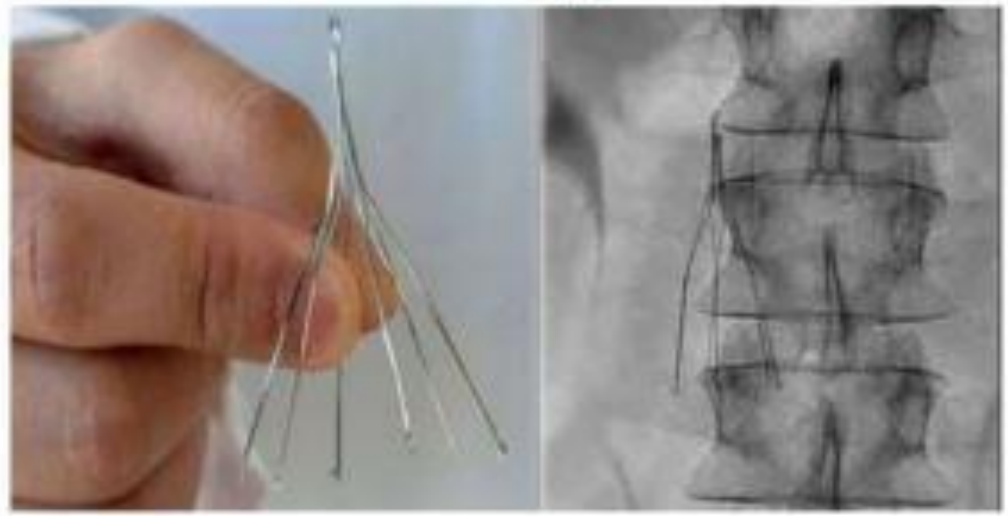
- Stop the drug
- Vitamin K
- Severe life-threatening hemorrhage → FFP + Vit K.
- CNS hemorrhage → Recombinant factor VIIa
- Prothrombin complex concentrates (PCCs) - Life-threatening bleeding, for immediate correction of INR. Contain 3 or 4 of the Vit K–dependent coagulation factors, proteins C and S.

Management of Acute DVT

Inferior vena cava filters

- ✓ ***Confirmed acute proximal DVT or acute PE in patient with contraindication for anticoagulation*** (most common indication for IVC placement)
- ✓ ***Recurrent thromboembolism while on anticoagulation***
- ✓ ***Active bleeding complications requiring termination of anticoagulation therapy***
- ✓ Large, free-floating iliofemoral thrombus in high-risk patients
- ✓ Propagating iliofemoral thrombus while on anticoagulation





Management of Acute DVT

Endovascular Intervention

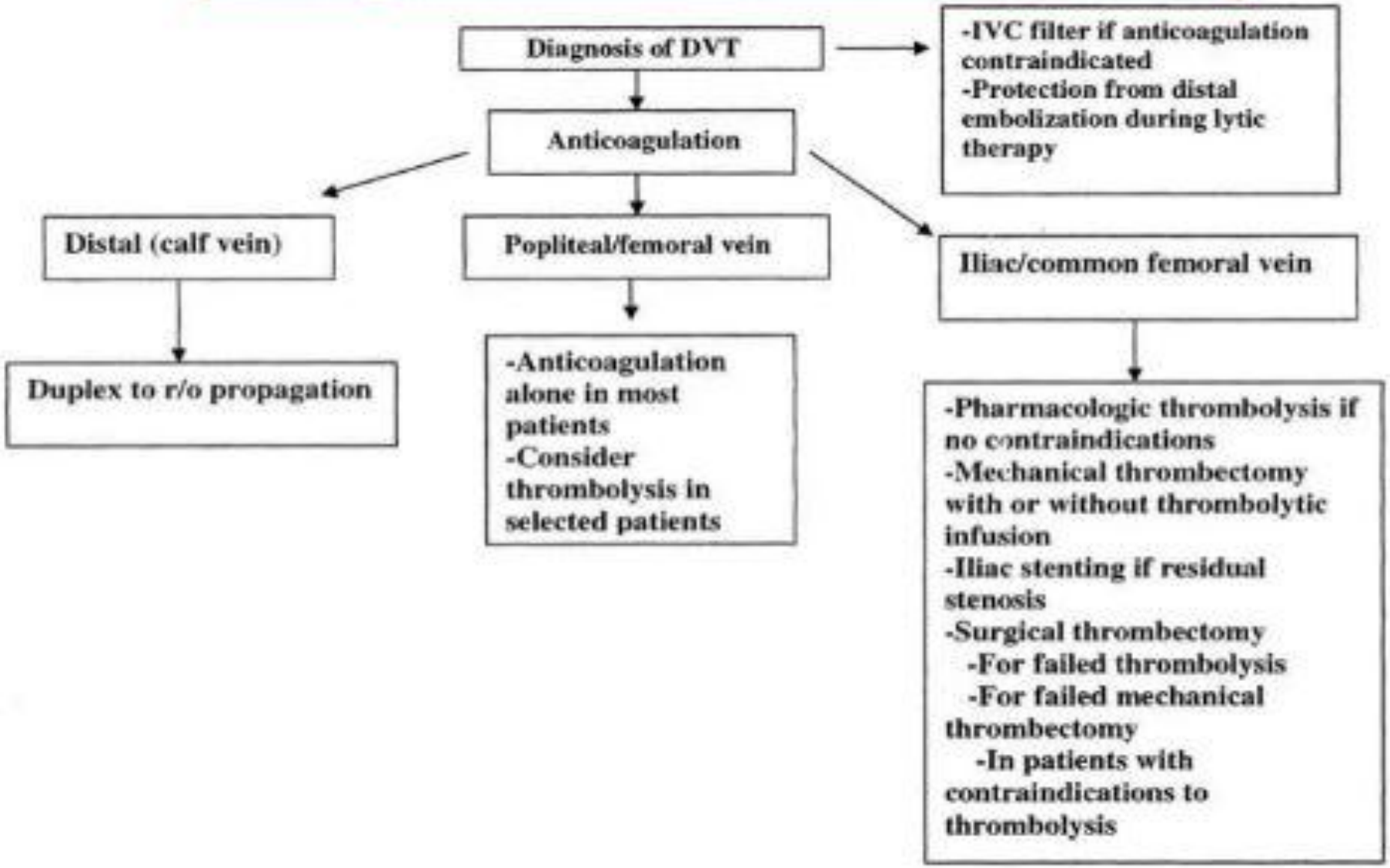
Most patients with DVT have absolute contraindications to thrombolytic therapy.

ACCP recommend thrombolytic therapy only for patients with **massive iliofemoral vein thrombosis** associated with limb ischemia or vascular compromise.

Surgical Thrombectomy

In patients with *massive swelling and phlegmasia cerulea dolens.*
Even when the bulk of the thrombus is not excessive, many patients with thrombosis are poor candidates for fibrinolysis because of recent surgery or trauma involving the CNS or other non-compressible areas.

Management of Acute DVT - Summary



REQUIREMENTS

1. Printed proforma containing 4 sections - Risk assessment, grouping of patient, contraindications for VTEP, VTEP modality.
2. Printed consent forms.
3. VTEP Algorhythms on Acrylic boards for ICU and Acute wards.
4. Pneumatic compression devices for ICU, Acute wards and OT.
   (Cost online 50000 – 1.5 lakhs per piece)
5. Graduated compression stockings. (INR 2000/-)
6. Inj Enoxaparin
7. Tab Ribaroxiban.

Flowtron DVT Pumps

The Flowtron DVT Pumps is the ideal standard pump for DVT therapy and compares with other Flowtron pumps as a versatile lightweight DVT pump. The Flowtron DVT Pump **more..** aids in the prevention of deep vein thrombosis (DVT)

Rs 98,000/Piece

Genotronics


THANK YOU
FOR YOUR
ATTENTION