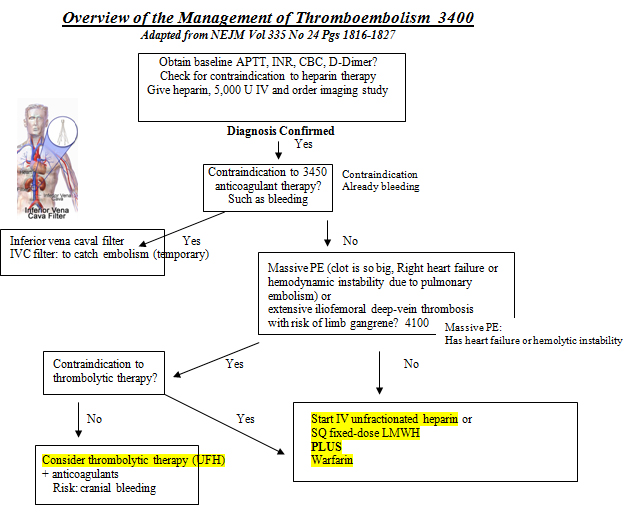
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| Drug | MOA | Advantage | Disadvantage | Dosing | Monitor | | ADR |
| Unfractionated Heparin (UFH)  Heparin | Binds to anti-thrombin 🡪 Inhibits Thrombin IIa and Xa  1:1 ratio  18 or more saccharides then bridge to antithrombin + thrombin  If 5 saccharides (pentasaccharide) binds to Xa | 1. Short half life- discontinue if there are major problems  2. **Safe in renal** dysfunction and ESRD (end stage renal disease) – not LMWH | 3. Unpredictable  4. Has to be continuous IV  (no PO)  5. Increase risk of  HIT & Osteoporosis with extended use b/c of long chain | 80/18  Initial: 80 units/kg/IV push  Infusion: 18 units/kg/hr  Round to 100  Use the Nomogram to increase or decrease dose over a span of 6 hours  Prophylaxis:  5,000 Units SQ q8-12 | **aPPT** (measures activated partial thromboplastin time Xa)  ACT at high doses (Activated Clotting time)  Signs and symptoms:  -BRBPR (bright red blood per rectum = bleeding in lower intestine)  -Intraocular  -Intracranial  -Retroperitoneal bleeding | | HIT (Heparin induced Thrombocytopenia)  Identify: If Platelets  < 100,000 or  less than 50%  then d/c all heparin  Treat OD: Protamine sulfate |
| LMWH  Low Molecular Weight Heparins  **Enoxaparin**  Dalteparin  Tinzaparin | Inhibits Xa:IIa (thrombin)  3:1 ratio  Binds less to thrombin IIa b/c it is short | 3. Predictable dose response (know ‘this’ dose works)  4. Can be used at home long t1/2=12hr  5. Decrease risk of HIT & osteoporosis compared to UFH  **Normally no lab monitoring** | 1. Long t1/2: **12 hr**  Also advantage  2. Renal Clearance – UFH is safe for renal  CrCl < 30 ml/min  Ok for pregnant  5. **If patient has history of HIT, don’t use** | DVT with or without PE (pulmonary embolism)  **1 mg/kg SC q12 hr**  1.5 mg/kg SC qday  Round to 10  Prophylaxis:  Enoxaparin for Orthopedic and High risk surgery  30 mg SQ q12h | **CBC < 1month**  **Obesity: > 150 kg (330 lb)**  Pregnancy: Check every trimester  Renal dysfunction: contraindicated if CrCl < 30ml/min | | Treat OD  No complete antidote: Protamine sulfate |
| Pentasaccharide  Fondaparinux  (Arixtra) | Inhibits Xa:IIa  **Xa: Thrombin**  **100:1 ratio**  b/c of short chain | 3. Predictable Dose response (no monitoring)  5. ‘No’ risk of HIT &  Osteoporosis  Compared to UFH | **1. long t1/2**  **(17 hr)**  **2. Contraindication if**  **CrCl < 30 ml/min**  4. SQ | Treat DVT/PE (pulmonary embolism)  < 50 kg (< 110 lb)  5 mg SC qday  50-100 kg (110 – 220 lb)  7.5 mg SC qday  > 100 kg (> 220 lb)  10 mg SC qday  Prophylaxis:  2.5 mg SQ daily | Does not alter aPTT or PT (coagulation test no required)  Renal dysfunction: contraindicated if CrCl < 30ml/min | | No antidote |
| Drug | MOA | Advantage | Disadvantage | Dosing | Monitor | | ADR |
| Warfarin | Prevents carboxylation (activation) of vitamin K dependent clotting factors | 4. PO  No effect on clotting factors that have already existed  Vit K clotting factors  Factor t1/2  **IIa** 100 hr  **VIIa**  3-6 hr  **IXa** 15-24hr  **Xa**  40 hr  (takes 100 hr =  4 days for all clotting factors to be inactive)  Protein S 60 hr  Protein C 9hr | Teratogenic  Drugs that **increase** INR: Bleeding  CYP2C9  **Amiodarone**  **Sulfonamides Bactrim Macrolides**  **Fluconazole**  **Metronidazole**  Ethanol (acute)  isoniazid  Thyroid hormone  Cimetidine  Erythromycins,  fluvastatin  Quinolones  Sertraline  Drugs that **decrease** INR: Clotting  CYP inducers  Barbiturates, Rifampin  Carbamazepine, Ethanol  **Antiplatelet drugs (does not increase INR but might increase bleeding)**  **Ginko Biloba**  **Aspirin**  **NSAID** | Patient Specific:  Age: > 65  Low dose  Nutrition, **CYP2C9**,  VKOR polymorph  **5mg/day**  Should initiate with concomitant UFH, LMWH or pentasaccharide and D/C injectable medication after at least 5 days of overlap and when warfarin is therapeutic (ie at goal INR) if patient has active clot  Duration  Unprovoked DVT  Time: 3 months  INR goal: 1.5 – 1.9  Provoked DVT:  Time: > 3 months  Recurrent DVT  Time: indefinite time  DVT + Cancer  Time: 3-6 months LMWH  Indefinite tme  When you discontinue warfarin, it also takes 3-5 days (if INR is 2-3) for normal coagulation to return  (ie, INR of 1) | INR (measures IIa,VIIa, Xa)  PT  Monitor  **Every Week**  (3 days – 1 month)  Adjust weekly warfarin dose by  5-20% based on INR values.  Continue warfarin for at least  3 months | | **S enantiomer**  **More potent**  **CYP2C9**  **monitor**  R enantiomer  Less potent  CYP1A2  Intracranial hemorrhage  Warfarin Induced skin necrosis  Hyperthyroidism:  Decrease warfarin  CHF b/c too much fluid in liver (busy) increase INR b/c too much warfarin  Pregnancy X  Stay consistent with Vitamin K1 intake  Food  Grapefruit Juice Cranberry Juice  Green tea  Garlic  Antidote  PO Vit K1  IV if emergency  SQ if can’t take PO  -Peak effect in 12 hr  -Check in 24 hr  -Vit K stays in body for up to 1 week |
| Drug | MOA | Advantage | Disadvantage | Dosing | Monitor | ADR | |
| Direct Thrombin Inhibitors (injectable)  Lepi**rudin**  (Refludan)  Treat HIT  Argatroban  treat HIT  Bivali**rudin**  (Angiomax)  Used in cardiac catheterization lab  Oral Thrombin Inhibitor  Dabigatran  (‘better’ alternative for warfarin) | Lepirudin irreversibly binds to thrombin  Agratroban is reversible  Bivalirudin is partially reversible  Inhibit thrombin w/o use of Antithrombin | **5. Used for patients with HIT (no thrombocytopenia induction)**  Good if patient is renally impaired  Inhibit both circulating and clot-bound thrombin  Used in patients with atrial fib. Date for VTE exists  No D-D interaction | 2. Dose adjustment required for renal/hepatic impairment  Agatroban + Warfarin  Falsely elevates INR  (INR increases w/ warfarin)  $$$ more than warfarin |  | PTT  Stomach upset | No antidote | |
| Thrombolytics  (fibrinolysis)  Tpa (AlterPlase)  Rpa (Reteplase)  TnKase (Tenecteplase) | Only drug that ‘breaks down’ fibrin. |  | Contraindication: Patients risk of bleeding outweighs benefit  **Intracranial hemorrhage 1 in 33 patients** |  |  | No antidote | |
| Xa Inhibitor (PO)  Rivroxaban (‘better’ alternative for warfarin) | Directly inhibits Xa without the use of antithrombin | **Onset: faster than Warfarin**  Predictable dose response  Little D-D interaction | $$$ more than warfarin |  |  | No antidote | |

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| Lab Values | Normal | VTE Goal |
| PT Prothrombin time | 10 – 13 seconds |  |
| INR International Normalized Ratio  INR = [PT (test)/PT (normal)] ^ ISI | 0.8 – 1.2 | 2 - 3 |
| aPTT Partial Thromboplastin Time | 25 – 35 seconds | 50-70 (based on table) |



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| Low Risk | Age <40  Minor Surgery  No Risk Factors | Calf vein DVT 2%  Proximal vein DVT 0.4%  Fatal PE <0.01% | No Specific  Prophylaxis |
| Moderate Risk | Age > 40 to 60 w/ No Risk Factors  Or  Minor Surgery w/ Risk factors | Calf vein DVT 10-20%  Proximal vein DVT 2-4%  Fatal PE 0.1-0.4% | LDUH (Q12): Low density Unfractioned Heparin  LMWH (low molecular weight Heparin) +  GCS (Graduated Compression Stockings)  or  IPC (Intermittent pneumatic compression) |
| High Risk | Age > 60  or  Age 40-60 w/ cancer, prior VTE or hypercoagulable disorder | Calf vein DVT 20-40%  Proximal vein DVT 4-8%  Fatal PE 0.4-1% | LDUH (Q8),  LMWH, (low molecular weight Heparin)  Or  IPC (Intermittent pneumatic compression) |
| Very High Risk | CHF  Cancer  Musculoskeletal disorders: stroke or spinal cord injury  Acute respiratory failure | Calf vein DVT 40-80%  Proximal vein DVT 10-20%  Fatal PE 0.2-5% | LMWH (low molecular weight Heparin) +  Fondaparinux, +  Warfarin,  or  IPC/GCS + LDUH |

***Methods of DVT Prophylaxis (sub-theraputic)***

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| **Method** | **Description** | |
| **Sequential Compression Devices (SCD)/Graded Compression Stockings (GCS)** | Start immediately before operation, and continue until fully  ambulatory, usually adjunctive therapy with pharmacologic therapy  Pros: if patient is already bleeding or has brain surgery | |
| **LMWH s** | Dalteparin 2500 IU SQ Daily (for medical patients)  5000 IU SQ daily (for surgery)  Don’t use if CrCl < 30 ml/min  Enoxaparin: 30 mg SQ Daily (CrCl 10-30 ml/min)  30 mg SQ Q12 hrs (Orthopedic and high risk surgery)  40 mg SQ Daily (Medical patients) | |
| **Pentasaccharides**  **Mini-dose Warfarin** | Fondaparinux 2.5 mg SQ Daily  Don’t use if CrCl < 30 ml/min or weight < 50kg  Start 1mg/day aimg for INR = 1.5 after operation (evidence is poor) | |
| Adjusted-dose perioperative **warfarin** | Start daily dose (5 mg) the day of or the day after operation;  adjust dose for INR 2-3  Cons: risk of bleeding in joints | |
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