VENOUS THROMBOSIS AND THROMBOEMBOLISM IN CHILDREN

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THROMBOEMBOLISM (VTE)

- incidence, risk factors, clinical manifestations, and diagnosis of VTE in children
- VTE in the newborn
- VTE in children with cancer

VTE IN CHILDREN

- The lower risk of VTE in children
- less commonly develop diseases causing damage to the vascular endothelium (eg, diabetes, dyslipidemias, hypertension).
- less frequently exposed to acquired prothrombotic risk factors (eg, oral contraceptives, hormone replacement therapy, pregnancy, smoking, malignancy, orthopedic surgery).
- Lower plasma concentrations of all vitamin K-dependent factors
- increased plasma concentrations of the thrombin inhibitor

RISK FACTORS IN CHILDREN

- Risk factors for VTE : stasis, endothelial injury, and hypercoagulability

- Central venous catheter (CVC related VTE), ~ 50% VTEs in children
- Inherited hypercoagulable state,
- Infection,
- Trauma,
- Immobility,
- Malignancy,
- CHD
- Chronic inflammatory conditions.

CLINICAL MANIFESTATIONS

- Venous thromboembolism (VTE), clinically presenting as DVT or PE
- usually asymptomatic ,
- pulmonary embolism (PE), 15% of VTE episodes
- Deep vein thrombosis(DVT)
- superior vena cava syndrome,
- swelling of the face,
- chylothorax,
- Renal vein thrombosis
- Portal vein thrombosis

VTE TREATMENT

The goals of treating VTE:

- Prevent local extension and embolization of the thrombus
- Aid in resolving the existing thrombus
- Prevent VTE recurrence
- Minimize long-term complications (post-thrombotic syndrome)

TREATMENT

- **Antithrombotic therapy** - unfractionated heparin (UFH),
  - low molecular weight heparin (LMWH) (Enoxaparin)
  - vitamin K antagonists (warfarin).

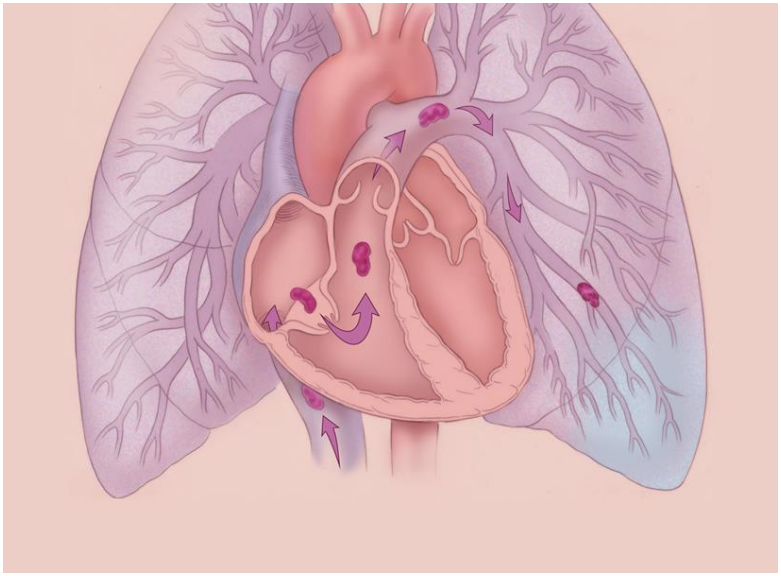
- provoked VTE: LMWH or UFH for 5 to 10 days, → three months LMWH or a VKA.
- Unprovoked VTE (no identifiable disorder or risk factor): LMWH or a VKA for 6 to 12 months.
- If VKA is used, the treatment should overlap with UFH/LMWH until the INR is in the therapeutic range (ie, 2.0 to 3.0) on two consecutive days.
- children with unprovoked VTE should be screened for inherited thrombophilia.
- **Thrombolytic therapy :** Tissue plasminogen activator [**tPA (***alteplase)]*

PULMONARY EMBOLISM

PE in pediatric patients:

1- In-situ pulmonary artery thrombosis (risk factors: CHD, lower age)

2- Classic pulmonary thromboembolism (risk factors: CVC, hospitalized children, cancer , immobility , nephrotic syn. Inflammatory conditions, SLE,)



- PE is rare in children.
- nonspecific and often mimic the clinical symptoms of the underlying disease.
- pleuritic chest pain, acute dyspnea, tachypnea, cough, hemoptysis, tachycardia,, hypoxia, and sudden collapse.
- Massive PE is rare(hypotension, hypoxemia, syncope, collapse)

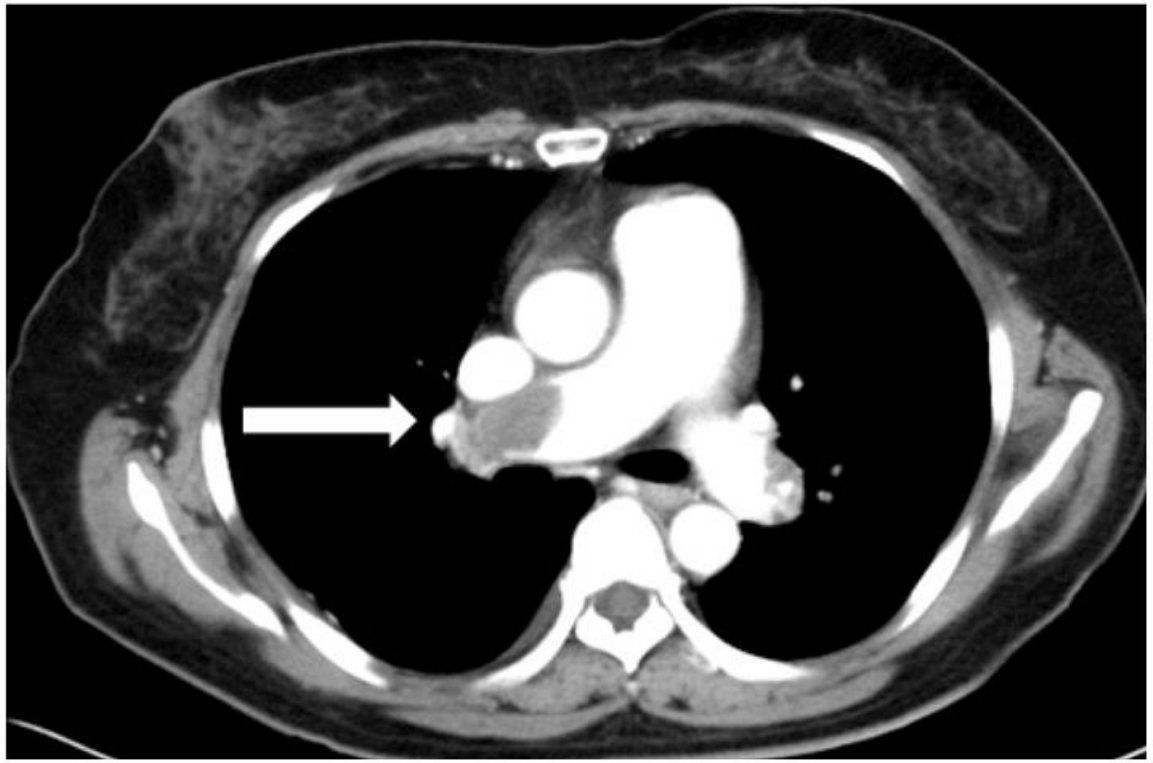
PE DIAGNOSIS:

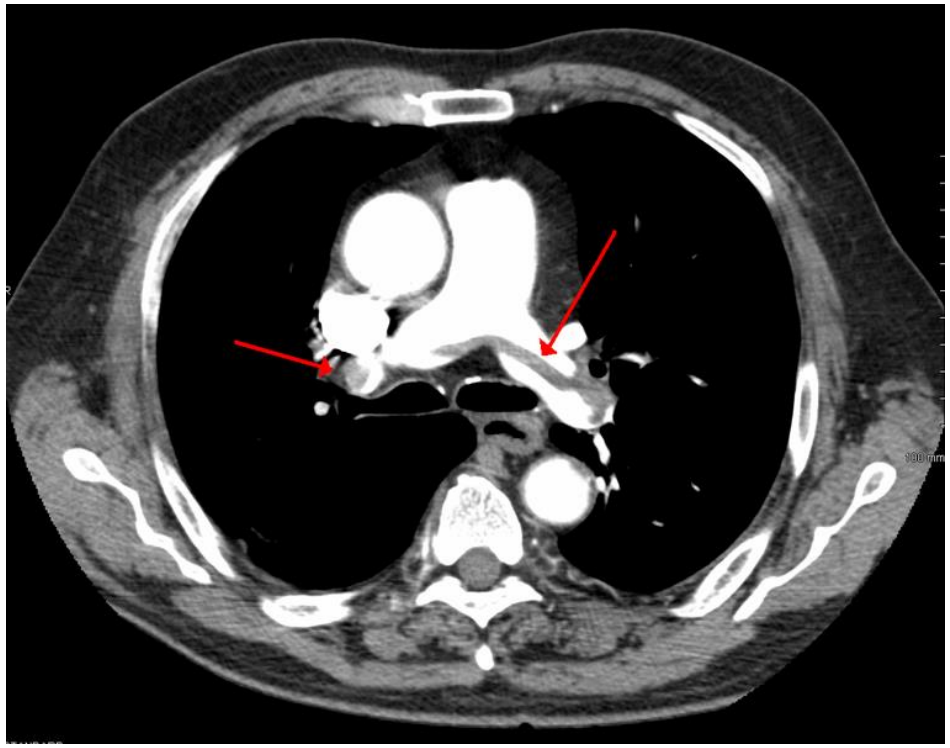
- DIAGNOSTIC CRIATERIA:
- Immobility
- Hypercoagulability state
- CVC
- Drug(estrogen)
- History of DVT

PE DIAGNOSIS

- Computed tomographic pulmonary angiography (CTPA) is the imaging modality of choice
- Pulmonary Angiography : gold standard
- Ventilation/perfusion scan: specific ,not sensitive
- D-Dimer: (neg. predictive value)
- ECG: normal ,RAD, RBBB,ST-T changes, normal
- CXR
- **Biomarkers :** cardiac troponin, brain-type natriuretic peptide,
- For venous thrombosis :Ultrasonography

PE





PE TREATMENT

- Provoked PE (CVC -related): Anticoagulation therapy 3 months
- Unprovoked PE: Anticoagulation therapy 6 to 12 months
- low molecular weight heparin [LMWH] ,(Enoxaparin)
- unfractionated heparin [UFH],
- Warfarin

- Direct oral anticoagulant (DOAC) ??/

- Thrombolytic agents (eg, tPA or urokinase) for extensive and hemodynamically compromising PE.

PE treatment , risk stratification

- Hypotension , CV collapse : medical Thrombolysis (rTPA +UFH/ LMWH) ± Mechanical thrombolysis, , follow with PT/PTT, fibrinogen ,plt
- No hypotension + evidence of RV strain/ biomarkers elevated : Medical Thrombolysis (rTPA+ UFH)
- Symptomatic but no evidence of RV strain/ normal biomarkers :Anticoagulant therapy (Heparin / LMWH)

- Heparin: 75 U/kg over 10 min, followed by 20 U/kg/h for patients >1 year, 28 U/kg/h for <1 year of age)
- Critical therapeutic level: 1.5 times the baseline / upper limit of normal range of aPTT
- LMWH(Enoxaparin): 1 mg/kg twice daily subcutaneously for patients >2 months of age, 1.5 mg/kg twice daily subcutaneously for patients <2 months of age)

LOW MOLECULAR WEIGHT HEPARIN

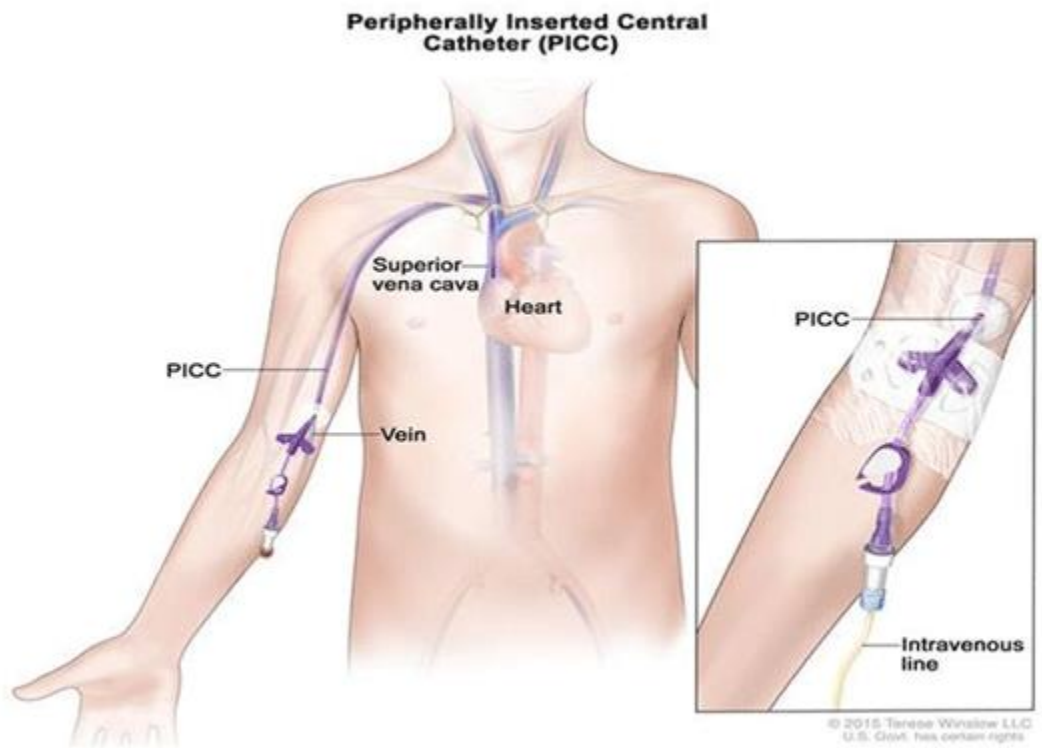
- More predictable anticoagulant response.
- Less laboratory monitoring and dose adjustment (anti-factor Xa assay, Samples should be taken four to six hours after the last subcutaneous injection; with this timing, the therapeutic range is between 0.5 and 1 units/mL.)
- treatment with UFH and particularly VKA requires frequent monitoring and dose adjustment.
- Less effect of diet
- Easier administration(subcutaneously),
- The therapeutic dose of LMWH is age dependent, (increased dose in newborns)
- Higher doses may also be necessary in critically ill children
- Reversal — (protamon; 1 mg protamine sulfate can inactivate 100 units of LMWH.

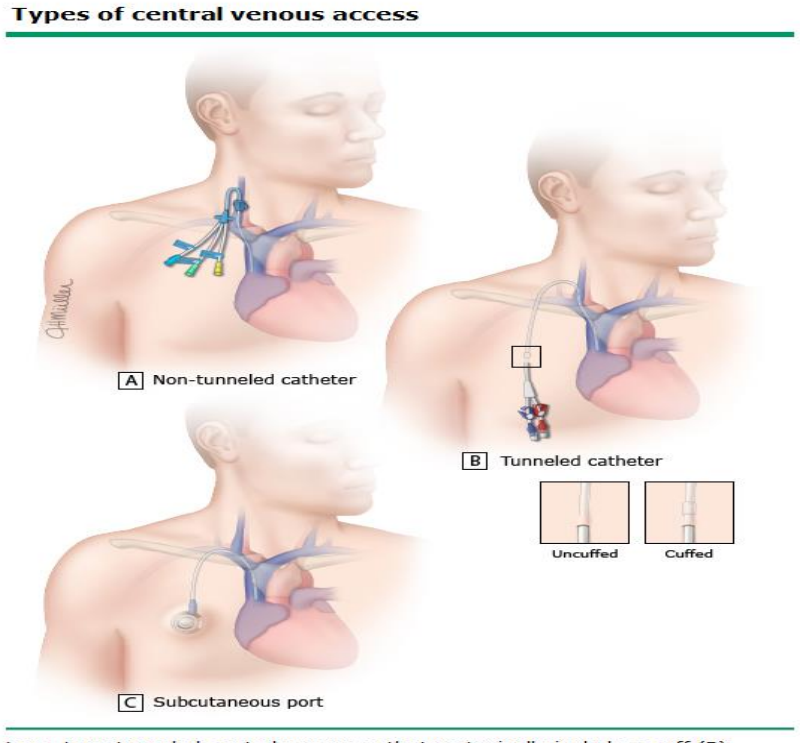
UNFRACTIONATED HEPARIN,/ WARFARIN

- **Heparin:**
- **Dose** : a loading dose of 75 units/kg IV over 10 minutes.
- Maintenance: Infants – 28 units/kg/ hr
- Children (≥1 year old) and adolescents: 20 units/kg/ hr
- **Adverse effects** : **Bleeding ,Osteoporosis, Heparin-induced thrombocytopenia**
- Reversal: **protamine sulfate**

- **Vitamin K antagonists: Warfarin**
- **Initial dose:** 0.2 mg/kg orally ,maximum 5 mg
- **Monitoring** :PT test

CENTRAL VENOUS ACCESS





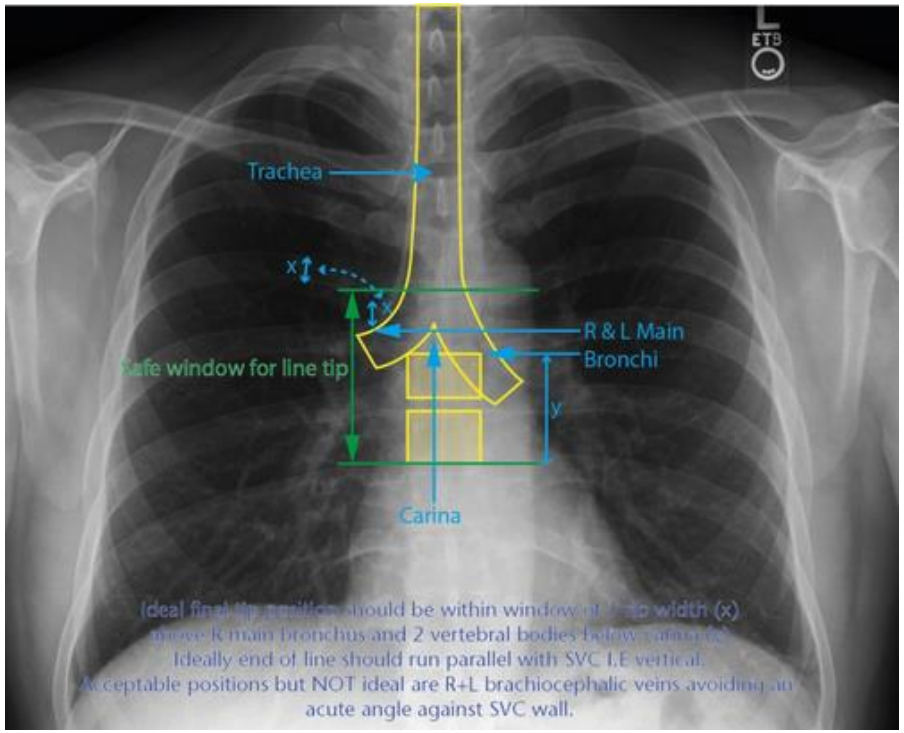
- Centrally inserted catheter, - Peripherally inserted catheter, - Port

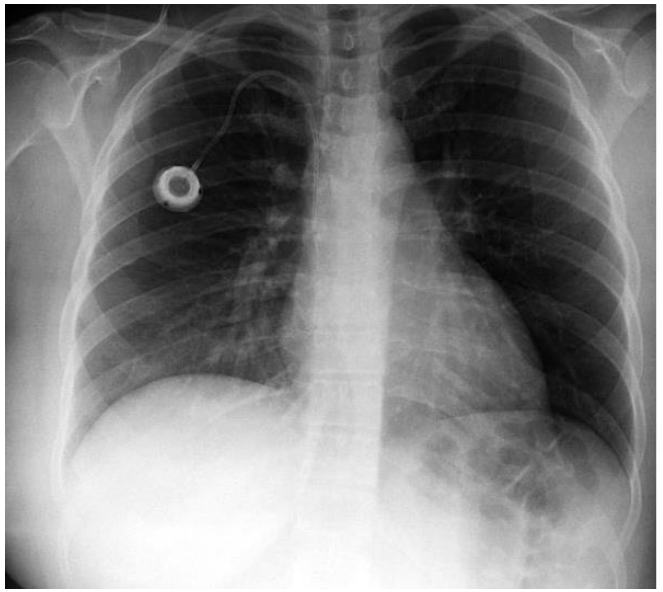
CATHETER-RELATED THROMBOSES

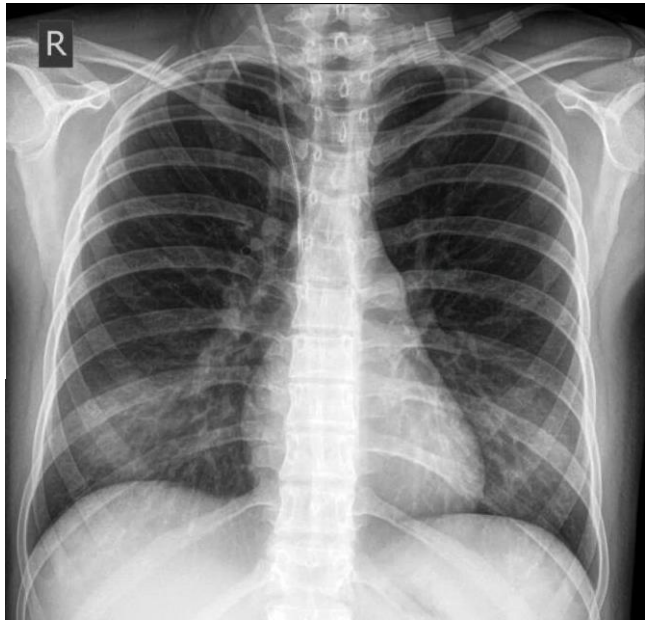
- Intravenous catheters cause endothelial trauma and vein wall inflammation, which can result in thrombosis.
- The majority of upper extremity deep vein thrombosis (DVT) events are due to peripherally inserted central catheters (PICCs).
- Risk factors for catheter-related DVT:

1-catheter malposition 2-catheter size 3- the presence of prothrombotic states 4- hormonal therapy

5- infusion of vesicant or irritant medications.


L
ETB
Trachea
x
x
R & L Main
Bronchi
Safe window for line tip
y
Carina
(Ideal final tip position should be within window of vessel width (x)
above R main bronchus and 2 vertebral bodies below carina (y).
Ideally end of line should run parallel with SVC I.E vertical.
Acceptable positions but NOT ideal are R+L brachiocephalic veins avoiding an
acute angle against SVC wall.

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CATHETER-RELATED THROMBOSES

- Symptoms and signs of catheter-related thrombosis:

  1- local effects of the thrombus (phlebitis, venous obstruction)

  2- Embolization to the pulmonary circulation,

  3- Paradoxically to the systemic circulation via a PFO.

- clinically silent and usually occur in the first 7 to 14 days from the time of catheter placement.
- Most PICC-related DVT occurs at the junction of the axillary and subclavian veins

TREATMENT

- The decision depends on whether: the CVC is functioning,
- : the VTE is symptomatic,
  : how critical central venous access is in the child's management,
  :the potential difficulty of obtaining new venous access

- Symptomatic care and anticoagulation for a minimum of three months.
- The treatment of PICC-related DVT is similar to that of other catheter-related DVT.

CVC-RELATED VTE

- removal of the CVC???.
- **CVC is not functioning or no longer necessary**: it should be removed.
- **Asymptomatic VTE + need for CVC**: keep the CVC in place + anticoagulation and monitoring for symptom development.

  → Symptoms associated with the VTE: removal of the CVC.

- **For functioning PICCs, routine removal in the setting of DVT is not recommended, since reinsertion of a catheter in the contralateral upper extremity is associated with high risk of thrombosis.**

- CVC-related VTE who continue to have their CVC in place : prophylactic doses of LMWH , until the CVC is removed.
- The risk of embolization of thrombus during catheter removal has not been well studied, but clinical practice suggests that overt embolization is low.

BLOCKED CENTRAL VENOUS CATHETER: THROMBOLYTIC THERAPY

- **Systemic thrombolysis , Catheter-directed thrombolysis**
- Blocked central venous catheter — ------- recombinant tPA (alteplase) :
- **Major vessel occlusion** —----------systemic or catheter-directed thrombolytic therapy

- Thrombolytic therapy is **not** recommended in patients with right-to-left cardiac shunts because of the risk of arterial emboli to the central nervous system.
- The major complication of thrombolytic therapy is bleeding. thrombocytopenia, vitamin K deficiency, Fibrinogen level)

VENOUS THROMBOEMBOLISM PROPHYLAXIS

- Early mobilization
- Prophylactic pharmacologic therapy in children with **multiple** risk factors for VTE.
- Routine use of antithrombotic therapy is **not** recommended

VTE IN NEWBORN

- Newborn infants are at risk for thrombosis: plasma concentrations of procoagulant, anticoagulant, and fibrinolytic factors are altered as compared with older children and adults.
- The risk is dramatically increased by the presence of an indwelling catheter, or by medical conditions predisposing to thrombosis, including prematurity and sepsis.
- Most venous thrombi are asymptomatic/ loss of catheter patency/ symptomatic: swelling of the affected extremities
- Right atrial thrombosis: a new murmur, heart failure, or persistent sepsis, as well as malfunction of the catheter.
- The diagnosis of thrombosis is suspected based on risk factors and clinical symptoms, and confirmed by imaging
- Evaluation for prothrombotic disorders testing: for those with thrombosis that is not related to an indwelling catheter or is recurrent.

TREATMENT

- **Asymptomatic catheter-associated thrombosis**: conservative management with supportive care and close monitoring of the size of the thrombus.
- Initial treatment with anticoagulation is a reasonable alternative to conservative management, particularly if it is not feasible to remove the catheter due to the patient's clinical condition.
- **Symptomatic thrombosis:** anticoagulation , Central catheters associated with thrombosis should be removed, if possible.
- **Right atrial thrombosis is usually catheter-associated**: catheter should be removed+ anticoagulation therapy.
- Conservative management is a reasonable alternative if the neonate is asymptomatic and the thrombus has low-risk features.
- **The thrombus is compromising cardiac function:** thrombolytic therapy

THROMBOEMBOLIC DISEASE IN CHILDREN WITH CANCER

- More prevalence in ALL, sarcoma , lymphoma
- High risk patients : 1- Asparaginase, 2-Stroide, 3-Central venous catheter, 4-thorombophilic disease
- Clinical manifestation :Neurologic, Pulmonary, Cardiac, Upper/ lower extremities, CV line
- Treatment : challenging because of bleeding tendency
- For most children with cancer and TE: anticoagulation with LMWH.
- platelet counts monitoring
- Platelet counts <20,000/ml: LMWH is held

TREATMENT IN CHILDREN WITH CANCER

- VTE in children receiving asparaginase therapy:
- Asparaginase is withheld +Treatment with LMWH
- Once the child is stable, hematologic parameters normalize, and anti-Factor Xa levels are in a therapeutic range, asparaginase therapy is resumed
- LMWH therapy is continued for at least three months or until the course of asparaginase is completed
- Asymptomatic right atrial thrombus with low-risk features: conservative management +removal of the central venous catheter (CVC)
- The CVC cannot be removed/high risk features: Anticoagulant therapy
- Prophylactic anticoagulation in children with cancer: additional risk factors


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