Clinical Practice Guideline: Primary Prophylaxis of Venous Thromboembolism (VTE)

Preface: This guideline provides evidence for the assessment of VTE risk and prophylaxis for children and adolescents from 6 months to <16 years of age within Princess Margaret Hospital.

Background:

While the need for prophylaxis of VTE in adult medical and surgical patients is well established and risk factors for VTE in children and adolescents are known (Table 1), the indications for prophylaxis in children are less well defined.1,2 This is largely because there are 10-fold fewer episodes of VTE in children and the relative contribution of many risk factors is small (Table 1), making the benefit/risk of routine pharmacologic prophylaxis marginal and expensive.3-6

Education and knowledge of medical and nursing staff should be directed at non-pharmacologic avoidance of VTE as well as early recognition of VTE with limited use of anti-thrombotic agents.7

Table 1
Risk factors for venous thromboembolism in children and adolescents

<table>
<thead>
<tr>
<th>Central venous lines</th>
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<tbody>
<tr>
<td>Cancer and chemotherapy</td>
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<td>Immobility or prolonged bed rest</td>
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<tr>
<td>Inherited thrombophilia</td>
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<td>Nephrotic syndrome</td>
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<td>Major burns</td>
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<td>Major trauma</td>
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<tr>
<td>Congenital heart disease and associated surgeries</td>
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<tr>
<td>Cardiac catheterisation</td>
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<tr>
<td>Obesity</td>
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<tr>
<td>Surgery; especially orthopaedics and neurosurgery</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Oral contraceptive pill</td>
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<tr>
<td>Previous VTE</td>
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<tr>
<td>Family history of VTE</td>
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<tr>
<td>Medications e.g. asparaginase</td>
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</table>
Prevention of VTE during surgery, anaesthesia and ICU care:

A guideline for peri-operative prophylaxis of venous thrombosis in children has been developed in the United Kingdom by Jackson and Morgan (see addendum).

Few patients require prophylaxis with low molecular weight heparin (LMWH). It is appropriate to consider consulting a clinical haematologist to aid decision making.

Most indications are in patients with complex cardiac abnormalities/procedures and anti-thrombotic therapy should be directed by the treating specialist. There are insufficient data for useful guidelines to be written for VTE prophylaxis, including peri-operative prophylaxis, in patients with other rare paediatric conditions such as sickle cell disease, acute lymphoblastic leukaemia and Proteus syndrome which may have an inherent risk of VTE.

Evidence-based guidelines from the American College of Chest Physicians for antithrombotic therapy in children were updated in 2008 and give the most comprehensive guidance for those with complex issues. This information can be found by following this link: Chest 2008;133:887S-968S. These patients should be managed individually by their primary consultant in liaison with the anaesthetist, surgeon and haematologist.

Management:

**General measures**

Both dehydration and immobility are independent risk factors for thrombosis. Therefore, all patients should be kept well hydrated with oral or IV fluids as necessary and should be mobilised as early as possible.

**Graduated compression stockings**

These reduce the overall cross sectional area of the limb, increase linear velocity of venous flow, reduce venous wall distension and improve valvular function.

*Knee length* is as effective as above knee.

Their limiting factor is size. They are made in S, M, L, and XL; regular and long; light to firm support. Measurements are taken from thigh, calf, ankle, and foot. It is therefore impossible to give an age limit, however, is most likely that these where needed would only be suitable for larger or adolescent patients.

[Measurement Guide](#) for compression stockings

[Guide to the Application and Use](#) of compression stockings
Flowtron Boots

These are available in 2 sizes for up to calf size of 43 cm circumference. Use therefore according to fit.

Contraindications
- Inadequate fit.
- Known DVT or phlebitis.
- Ischemic disease.
- Any local condition such as recent skin grafts, leg wounds or dermatitis.

Enoxaparin (Clexane)

Dose:
1. Child 6 months – 18 years: 0.75mg/kg/dose twice daily, subcutaneous.
2. Maximum dose 20 mg twice daily, subcutaneous.
3. Adult dosing of 40 mg daily can be given where felt appropriate for adolescents of >40 kg weight.
4. These doses have been reached by measurements of factor Xa levels and peak levels occur 4 hours post-subcutaneous injection (prophylactic target range for anti-Xa levels = 0.1–0.4 units/ml).
5. Given 2 hours pre-op in high-risk patients if possible otherwise on induction by vertical subcutaneous injection into the lower abdomen.
6. If using a regional technique Clexane must be omitted until after the procedure and the epidural catheter removed at least 12 h after Clexane administration.

Contraindications:
- Hypersensitivity.
- Previous heparin-induced thrombocytopenia (HIT).
- Platelets < 80 x 10^9.
- Congenital or acquired bleeding.
- Oesophageal varices.
- Active peptic ulcer disease.
- Renal or hepatic failure.
- Severe hypertension.
- Endocarditis.
- Surgery to brain, eye or spinal cord.

Precautions -
Review indications for prophylaxis daily and discontinue when mobile.

Where prophylaxis will be continued:
⇒ Monitor platelet function at initiation and thereafter twice weekly.
⇒ Check baseline clotting – if clotting is normal, further monitoring of factor Xa only if clinically indicated, i.e. bleeding.
⇒ Blood sample taken on day 1 and/or day 2 for determination of factor Xa level and platelet count. This should be drawn 4 hours after subcutaneous administration of low molecular weight heparin – samples sent to Haematology.
• Where a patient is currently under the care of a haematologist, please discuss proposed care with them.
• It is also likely that patients with previous DVT or HIT would have received care from a haematologist and this should be discussed with them.
• Patients with mechanical heart valves should be managed in conjunction with the haematology team using IV Heparin.

**Thrombophilia screening:**

There is currently no indication for thrombophilia screening in children with VTE or with a family history of thrombophilia except in the rare clinical scenario of neonatal skin necrosis to confirm or exclude homozygous deficiencies and prescribe appropriate treatment\textsuperscript{17-21}.

Knowing whether or not a child has an inherited thrombophilic defect does not aid decision making regarding primary prophylaxis of VTE. Indeed, even following an episode of thrombosis, treatment and prophylaxis recommendations are not altered by thrombophilia screening results.

Routine thrombophilia screening is not recommended prior to prescription of the oral contraceptive (OCP) in adolescents since the increase in risk of VTE does not outweigh the benefit of OCP use.

**Early recognition and treatment of venous thromboembolism**

While not the remit of this guideline, it must be acknowledged that simply because of the relative rarity of paediatric VTE, many episodes will not be prevented and education and knowledge are required for the recognition of clinical signs and symptoms of VTE in neonates, children and adolescents. Early and appropriate investigations for diagnosis, therapy and secondary prevention of VTE are essential to reduce the morbidity from post-phlebitic syndrome\textsuperscript{20}. Antithrombotic therapy in neonates and children is a complex issue and the reader is referred to Monagle et al Chest 2008\textsuperscript{10} for treatment guidelines and advised to manage patients in consultation with a clinical haematologist. These guidelines also address prophylaxis and treatment of arterial thrombosis.

**References:** Click [here](#) for list.
ADDENDUM: VTE Risk Assessment Score

| Age (see Note 1) | Child (6 months - pre puberty) = 0 Points
| | Adolescent (puberty onwards) = 2 Points

| Congenital Diseases (See Note 2) | 1 Point for each of the following:
| | Congenital heart disease
| | Inherited thrombophilic conditions
| | Certain metabolic diseases
| | Certain malformations

| Pre existing medical problems (See Note 3) | 1 point for each of the following:
| | Inflammatory diseases
| | Connective tissue diseases
| | Previous thrombosis at any site

| Current medical problems | 1 point for each of the following:
| | Active infection (Meningitis/Sepsis/Varicella/HIV)
| | Major trauma and/or Burns
| | Immobility
| | Pregnancy
| | Obesity
| | Heparin Induced Thrombocytopenia (NB: enoxaparin contraindicated)

| Medication | 1 point for each of the following:
| | Oral contraceptive
| | Asparaginase
| | Steroids
| | TPN
| | Smoker

| Iatrogenic issues | 1 point for each of the following:
| | Shunt/Stents/PICC line
| | 2 points for Central Venous Catheter

TOTAL SCORE =
Note 1 - AGE

It is impossible to give an age range for childhood or adolescence because puberty varies from individual to individual. It is assumed that the increased thrombotic risk of adulthood arrives with sex steroid release. Therefore for this guideline, adolescence is indicated by children who have started their growth spurt with evidence of breast development and onset of menstrual cycle in girls, and voice breaking in boys.

Note 2 – CONGENITAL DISEASES

'Congenital heart disease' implies patients who have previously undergone heart surgery but are now considered to be corrected. Children who have ongoing cardiac disease, such as prosthetic valves or cardiomyopathy are a separate population and will usually be having their elective surgery at specialist centres. For more detailed instructions in this patient group the authors direct the reader to Chest 2008;133;887S-968S

'Pre-existing thrombophilic conditions' are the following:
- Antiphospholipid antibodies
- Antithrombin deficiency
- Factor II (G20210A) (=prothrombin)
- Factor V Leiden
- Hyperhomocysteinaemia
- Increased factor VIII (>1500 IU·L⁻¹ unrelated to acute phase reaction)
- Increased lipoprotein
- Protein C deficiency
- Protein S deficiency
- Sickle cell anaemia
- Polycythaemia

'Certain metabolic diseases' include carbohydrate deficient glycoprotein syndrome (CDG)
'Certain malformations' includes anal atresia, porencephaly, and the Kasabach–Merritt association (Kaposi haemangioendothelioma and thrombocytopenia)

Note 3 – PRE-EXISTING MEDICAL PROBLEMS

'Inflammatory diseases' are Kawasaki's disease, ulcerative colitis, Crohn's disease, nephrotic syndrome, etc.

'Connective tissue diseases' are SLE, JIA etc.

'Previous thrombosis at any site' includes previous DVT, portal vein thrombosis, Purpura fulminans
### Prophylaxis Guide

#### SURGERY

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<thead>
<tr>
<th>Score</th>
<th>1 – 2</th>
<th>3-5</th>
<th>6+</th>
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<tbody>
<tr>
<td><strong>Low Risk</strong></td>
<td>Surgery of any type</td>
<td>Any surgery &lt;30 mins duration</td>
<td>Any surgery &lt;30 mins duration</td>
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<tr>
<td>▪ Ensure good hydration</td>
<td></td>
<td></td>
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<tr>
<td>▪ Early mobilisation</td>
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<tr>
<td><strong>Medium Risk</strong></td>
<td>Any surgery &gt;30 mins duration</td>
<td>Any minor surgery &gt;30 mins duration</td>
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<tr>
<td>▪ Graduated compression stockings</td>
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<td>▪ Flowtron boots in theatre</td>
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<tr>
<td>▪ Plus measures for low risk group</td>
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<tr>
<td><strong>High Risk</strong></td>
<td>Major orthopaedic surgery</td>
<td>Any major surgery</td>
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<tr>
<td>▪ ENOXAPARIN</td>
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<tr>
<td>▪ Plus measures for medium and low risk groups</td>
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#### ICU

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<tr>
<th>Score</th>
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<th>3-5</th>
<th>6+</th>
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<tbody>
<tr>
<td><strong>Low Risk</strong></td>
<td>Not ventilated or Intubated &amp; ventilated &lt; 48 hours</td>
<td>Not ventilated or Intubated &amp; ventilated &lt; 48 hours</td>
<td>All 6+ patients at least medium risk</td>
</tr>
<tr>
<td>▪ Ensure good hydration</td>
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<tr>
<td>▪ Early mobilisation</td>
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<tr>
<td><strong>Medium Risk</strong></td>
<td>Intubated &amp; ventilated &gt; 48 hours</td>
<td>ICU bed rest &gt;48 hours or intubated and ventilated &gt; 48 hours</td>
<td>Not ventilated</td>
</tr>
<tr>
<td>▪ Graduated Compression Stockings</td>
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<td>▪ Plus measures for low risk group</td>
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<tr>
<td><strong>High Risk</strong></td>
<td>Intubated and ventilated</td>
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<tr>
<td>▪ ENOXAPARIN</td>
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<tr>
<td>▪ Flowtron boots if enoxaparin contraindicated</td>
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<tr>
<td>▪ Plus measures for medium and low risk groups</td>
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